SECTION THREE

PROFILE OF THE PHARMACEUTICAL INDUSTRY

This profile of the U.S. pharmaceutical industry provides descriptive and statistical information necessary for developing the EA methodology presented in Section Four and for interpreting its results. This section is organized into three subsections that address the principal determinants of supply and demand for U.S. pharmaceuticals and present key industry statistics. The section begins with an introduction to the pharmaceutical industry—its functions, products, regulatory environment, and manufacturing processes. Section 3.2 presents basic facility, owner company, and parent-level statistics including number of facilities, employment, value of shipments, international trade, production costs, and baseline financial conditions. Finally, Section 3.3 discusses market structure and demand in the pharmaceutical industry. Key topics such as barriers to entry, vertical integration, industry concentration, and the price elasticity of pharmaceutical demand are covered. The section concludes with an analysis of the industry's ability to raise prices in response to increased regulatory costs.

3.1 STRUCTURE OF THE PHARMACEUTICAL INDUSTRY

Any EA requires an understanding of the basic structure of the affected industry so that impacts on specific members, functions, or processes can be identified, distinguished, and estimated. At its core, the pharmaceutical industry is the collection of commercial enterprises engaged in the discovery, manufacture, and sale of drugs. As such, the industry plays a central role in public health—it produces the steady stream of medicines needed to prevent, diagnose, and treat disease; to extend life and improve our quality of life; and to continually advance the quality, breadth, and effectiveness of available health care. Producing this steady stream of medicines involves a range of activities:

- Research and development (R&D)—to discover, enhance, and devise reliable manufacturing processes for drugs.
- Bulk manufacturing—to produce large volumes of drug ingredients.

- Finished dosage form manufacturing—to combine drug ingredients in a form suitable for sale and use.

- Marketing—to promote and sell drugs (e.g., by informing health care providers and consumers of their availability, features, and proper use).

Individual companies in the pharmaceutical industry may specialize in any one or more of these activities. In addition, they may specialize in researching, manufacturing, and/or marketing any one or more of the major types of drugs—new prescription drugs, generic prescription drugs, and over-the-counter (OTC) drugs—or in any one or more therapeutic area. Indeed, pharmaceutical companies are a diverse lot, including companies that focus on just one function (e.g., bulk manufacturing) for one product group (e.g., OTCs), companies that combine a couple of or a few functions for more than one product group, and companies that perform all functions for all types of products. In general, smaller pharmaceutical companies tend to specialize in the manufacture or sale of bulk ingredients or generic products, or in the development of one or a few very specific products (e.g., bioengineered anticancer drugs). Many large pharmaceutical companies, on the other hand, are "innovative" companies (i.e., that discover, produce, and/or market new drugs) that also produce generic and OTC drugs.

Although most people think of drugs as chemicals used to treat human disease, these products encompass a broad range of substances, including synthetic/semisynthetic chemical, biological, recombinant DNA (bioengineered), and radioactive products; drugs for human and veterinary use; and therapeutic drugs (used to prevent, ameliorate the symptoms of, or treat disease) and diagnostic substances (used to diagnose disease or monitor health status). Thus, this analysis encompasses all these types of products. For the purpose of this EA, biological products, veterinary products, and diagnostic products are considered subsets of new and generic drugs.

The pharmaceutical industry is regulated by a variety of state and federal agencies that play a major role in nearly all pharmaceutical activities. At the core of pharmaceutical regulation is FDA, which is charged with ensuring the safety and effectiveness of drugs intended for human and animal use. To this end, FDA reviews drugs before they reach the market, monitors clinical trials, dictates labeling requirements, specifies acceptable manufacturing practices, and conducts postmarket surveillance. Other federal and state agencies, such as the Occupational Safety and Health Administration (OSHA) and EPA, regulate the health, safety, and environmental practices of the pharmaceutical industry. Federal and state governments also exert

considerable influence on the industry by serving as major third-party payers of prescription drugs under Medicare and Medicaid programs (see Section 3.3.2), purchasing large quantities of pharmaceutical products through the U.S. Public Health Service and the Veterans Administration (VA), sponsoring pharmaceutical R&D through the National Institutes of Health (NIH), and crafting tax policies that can influence product development.

The central goal of this government oversight and influence is to achieve socially desirable ends (e.g., product safety, a clean environment, etc.) without excessively compromising the industry's ability to discover, produce, and sell drugs needed to serve the nation's public health interest. To assess potential impacts of EPA's proposed effluent limitations guidelines and standards on individual components of the pharmaceutical industry and the industry as a whole, this EA will segment the pharmaceutical industry by:

- U.S. Department of Commerce SIC code (SICs 2833, 2834, 2835, and 2836).
- Major type(s) of drugs produced.
- Principal manufacturing processes.

Sections 3.1.1, 3.1.2, and 3.1.3 describe these three segmentation schemes in more detail.

3.1.1 Department of Commerce SIC Codes

As noted in Section Two, U.S. Department of Commerce divides the pharmaceutical industry into four 4-digit SIC codes:

- SIC 2833 Medicinal and Botanical
- SIC 2834 Pharmaceutical Preparations
- SIC 2835 In Vitro and In Vivo Diagnostic Substances
- SIC 2836 Biological Products, Except Diagnostic Substances

This segmentation scheme is mainly useful in interpreting Commerce data on pharmaceutical establishments, employment, production, consumption, and the like. These data are presented and discussed throughout the remainder of this document.

3.1.2 Major Types of Drugs Produced

Currently, the pharmaceutical industry produces more than 110,000 pharmaceutical products.[1] Most commonly, these products are classified as new (patented, branded) drugs, generic drugs, or OTC drugs. FDA defines these product types as follows:

- A new drug is an entirely new molecular entity (NME); a new ester, salt, or other noncovalent derivative; a new formulation; for a new indication; or a new combination (see Figure 3-1).
- Generic drugs are equivalent versions of previously marketed, patented drugs and generally appear on the market several years after patent expiration.
- OTC drugs are available without a prescription and generally undergo a less rigorous review process than do prescription drugs. Examples of OTC drugs include aspirin, cough medicines, and home pregnancy tests.

As can be seen in Figure 3-2, new drugs accounted for the majority (62.3 percent by total dollar volume) of industry sales in 1991. OTC drugs accounted for 27.5 percent of sales and generic drugs made up the remaining 10.2 percent. More recent independent data were not available, but many industry analysts have observed a steady increase in the generic and OTC shares of the total pharmaceutical market. Most attribute this trend to cost pressures (encouraging greater use of generics) and numerous conversions of prescription drugs to OTC products. It should be noted, too, that because prescription pharmaceuticals are considerably more expensive than generic and OTC products, dollar sales volume figures for these product groups do not match the frequency of their usage. By unit sales or number of prescriptions filled, generic drugs are more dominant than their dollar sales suggest. In 1991, for example, generic drugs accounted for 34 percent of all prescriptions filled, but only 19.1 percent of total prescription drug sales, and just 12.6 percent

[1] As cited in Research Triangle Institute (RTI), 1993. *Economic Analysis of Effluent Guidelines Regulations for the Pharmaceutical Industry.* Draft Report. Contract No. 68-C8-0084. Research Triangle Park, NC: RTI.

New molecular entity (NME). A drug for which the active moiety (either as the unmodified base compound or an ester, salt, clathrate, or other noncovalent derivative of the base compound) has not been previously approved or marketed in the United States for use in a drug product, either as a single ingredient or as part of a combination product, or as part of a mixture of stereoisomers.

New ester, salt, or other noncovalent derivative. A drug for which the active moiety has been previously approved or marketed in the United States, but for which the particular ester, salt, clathrate, or other noncovalent derivative, or the unmodified base compound is not yet approved or marketed in the United States, either as a single ingredient, part of a combination product, or part of a mixture of stereoisomers.

New formulation. A new dosage form or formulation, including a new strength, where the drug has already been approved or marketed in the United States by the same or another manufacturer. The indication may be the same as for the already marketed drug product or may be new.

New combination. A drug product containing two or more active moieties that have not been previously approved or marketed together in a drug product by any manufacturer in the United States. The new product may be a physical or a chemical (ester or noncovalent) combination of two or more active moieties.

New indication. The product duplicates a drug product (same active moiety, same salt, same formulation, or same combination) already approved or marketed in the United States by the same or another firm except that it provides for a new use.

Figure 3-1. New drug definitions.

Source: U.S. FDA, 1992. *Office of Drug Evaluation: Statistical Report*. Rockville, MD: U.S. FDA.

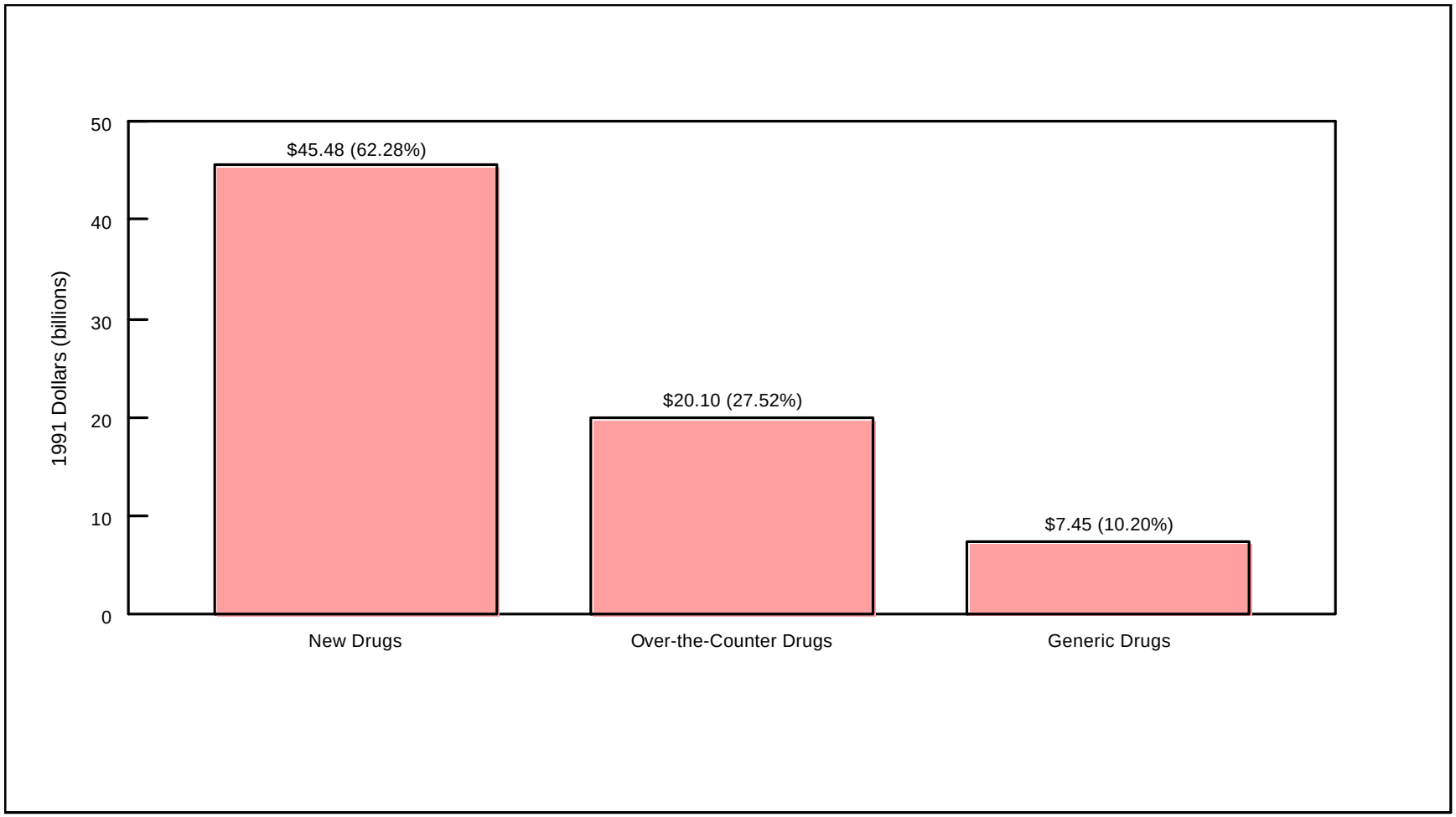

Figure 3-2. U.S. Drug Sales by Major Drug Type: 1991 (billions of dollars).

Source: NatWest, 1992. *The U.S. Generic Drug Industry*. New York: NatWest. U.S. Department of Commerce, 1993. *U.S. Industrial Outlook: 1993.* Washington, DC: U.S. Government Printing Office.

of total pharmaceutical sales.[2] Consistent with the observed trend toward greater use of generics, the trade association Pharmaceutical Research and Manufacturers of America (PhRMA) states that the generics share of the market (by number of prescriptions filled) rose from about 34 percent in 1991 to nearly 43 percent in 1995.[3]

Not surprisingly, the three major drug types face differing market conditions. For branded, patented drugs, the presence of patents and other barriers to market entry can create monopolistic conditions. In some therapeutic areas (e.g., HIV infection), monopolistic or semimonopolistic conditions prevail due to the lack of a wide array of effective drugs. In many therapeutic areas, however, competition ranges from moderate to intense due to the availability of several drugs (both branded, patented drugs and generic versions of branded drugs whose patents have expired) with similar therapeutic profiles. When AZT entered the human immunodeficiency anti-virus (HIV) market, for example, no approved alternatives were available and AZT enjoyed monopolistic conditions. When Biaxin® (clarithromycin) entered the upper respiratory anti-infective market, in contrast, the availability of a wide array of other broad-spectrum antibiotics (including a variety of branded and generic penicillins, cephalosporins, quinolones, and erythromycins, among others) meant that Biaxin® faced considerable competition in its market.

Even when multiple products compete intensely, purely classic competitive conditions rarely prevail in the prescription drug market because clinical considerations often outweigh unit price. In the treatment of upper respiratory infections, for example, physicians take into account the type of bacterium likely to be causing an individual patient's infection, the possibility of bacterial resistance to older antibiotics, the dosage schedule (patients are more likely to comply with therapy and show clinical improvement if they can take fewer doses), the likelihood of side effects, effectiveness in patients with concomitant diseases or in those taking other drugs, and so on. Due to factors such as these, the total cost of treatment (including the cost of retreatment if drug failure or relapse occurs, the cost of revisits to discuss side effects, etc.) is sometimes lower when higher unit-cost patented drugs are used than when low unit-cost generic drugs are used. In this

[2] NatWest, 1992. The NatWest Investment Banking Group. *The U.S. Generic Drug Industry*. New York: NatWest.

[3] PhRMA, 1996. *Generics' Share of U.S. Market, 1984-1995*. Document Number 5022. Pharmaceutical Research and Manufacturers of America.

context, Biaxin® garnered significant market share despite the availability of inexpensive generic penicillins and erythromycins.

In the OTC market, on the other hand, consumers make drug choices themselves. Because of this, and because of the availability of many branded and generic versions of products in most categories (e.g., analgesics, cough/cold remedies, etc.), price plays a more central role. Competition among and within the three drug groups and other issues concerning market structure in the pharmaceutical industry are discussed in more detail in Section 3.3. The following three subsections examine the major drug groups and regulations that affect their manufacture and sale.

3.1.2.1 New Drugs

About 90 percent of all drugs marketed since 1938 were new drugs at the time of their introduction. This "new" drug status is not permanent, however. Although most of those introduced in the 1980s and 1990s are currently available as branded drugs, with no generic equivalents yet on the market, many of the older drugs, although "new" when first introduced, are now old enough to have lost their patent protection. Despite the availability of generic equivalents, many of these off-patent branded products remain on the market. Other formerly "new" branded drugs are no longer available, however, having been entirely supplanted by generic equivalents or newer drugs with improved therapeutic profiles.

The process of bringing a new drug to market is lengthy and complex (see Figure 3-3). The process begins with discovery experiments in which scientists screen existing substances for therapeutic or diagnostic potential, modify existing substances to create new substances with desired therapeutic or diagnostic properties, or attempt to create (through chemical synthesis, genetic manipulation, or biological processes) entirely new substances with therapeutic or diagnostic properties. When a drug seems to hold promise, scientists conduct more extensive laboratory investigations to characterize the drug's physical properties as well as preclinical animal studies to determine how it affects living systems. If these studies are successful, the sponsoring pharmaceutical firm designs and initiates clinical studies in which the drug is given to humans. At this point, FDA becomes directly involved for the first time. It should be noted that very few substances

It takes 15 years on average for an experimental drug to travel from lab to medicine chest.
Only five in 5,000 compounds that enter preclinical testing make it to human testing.
One of these five tested in people is approved.

	Early Research/ Preclinical Testing		Clinical Trials: Phase I	Clinical Trials: Phase II	Clinical Trials: Phase III		Phase III		Phase IV
Years	6.5		1	2	3		2.5*	15 Total	Additional post-marketing testing required by FDA
Test Population	Laboratory and animal studies	File IND at FDA	20 to 80 healthy volunteers	100 to 200 patient volunteers	1,000 to 3,000 patient volunteers	File NDA at FDA	Review process/ approval		
Purpose	Assess safety and biological activity		Determine safety and dosage	Evaluate effectiveness, look for side effects	Verify effectiveness, monitor adverse reactions from long-term use				
Success Rate	5,000 compounds evaluated		5 enter trials				1 approved		

* Average for 1990-1994. In 1994, the average approval time was 1.5 years.

Figure 3-3. The drug development and approval process in the 1990s.

Source: Beary, John F., 1996. *The Drug Development and Approval Process*. Pharmaceutical Research and Manufacturers of America.

make it this far. PhRMA estimates that of about 5,000 substances screened, only 5 make it to human testing—and just 1 makes it to market.[4]

Before any new drug can be tested on humans, the drug's sponsor must submit an investigational new drug (IND) application to FDA that summarizes the preclinical work, lays out a plan for how the drug will be tested in humans, and provides assurances that appropriate measures will be taken to protect study participants. Unless FDA decides that the proposed study is unsafe, clinical testing may begin 31 days after the IND application is submitted to FDA. While clinical trials progress through several phases aimed at establishing safety and efficacy, the manufacturer develops the processes necessary to produce large quantities of the drug that meet quality standards for commercial marketing.

When all this work has been done, the pharmaceutical firm submits a new drug application (NDA) that includes the information FDA needs to determine whether the drug is safe and effective for its intended use and whether the manufacturing process can ensure its quality. Because they have never been marketed before, new drugs receive the most scrutiny from FDA and undergo a lengthy review process.[5] Throughout this process, drug sponsors typically interact with FDA to answer questions and address concerns. After completing its review, FDA responds to each NDA with an approval letter (approving the drug for manufacture and sale), an approvable letter (indicating that the drug will be approved if certain issues are addressed), or a not approvable letter (indicating that the drug may not be manufactured or sold).

According to FDA data, the agency has approved an average of 90 new drugs each year since 1982 (see Figure 3-4). Approximately 26 percent of the new drugs approved each year are NMEs. The agency also approves, on average, some 1,207 new drug supplements, which describe proposed changes to an already

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[4] Moore, Judy, 1996. *The Pharmaceutical Industry.* National Health Policy Forum background paper. Washington, DC: The George Washington University.

[5] Under pressure to review NDAs faster, FDA has begun receiving payments from new drug sponsors to help cover reviewing expenses; authorized by the Prescription Drug User Fee Act of 1992, this program was expected to bring in $300 million over 5 years, at which point the program expired to allow time for a review of the program's effectiveness in speeding drug reviews (U.S. Department of Commerce, 1994. *U.S. Industrial Outlook: 1994.* Washington, DC: U.S. Government Printing Office). This program was reauthorized under the FDA Modernization Act of 1997. Citing FDA sources, PhRMA states that FDA's average review time for NDAs declined from about 30 months to about 19 months between 1992 and 1995 (PhRMA, 1996. FDA Approves 28 New Drugs; Review Time is 19.2 Months. *New Drug Approvals in 1995.* Pharmaceutical Research and Manufacturers of America).

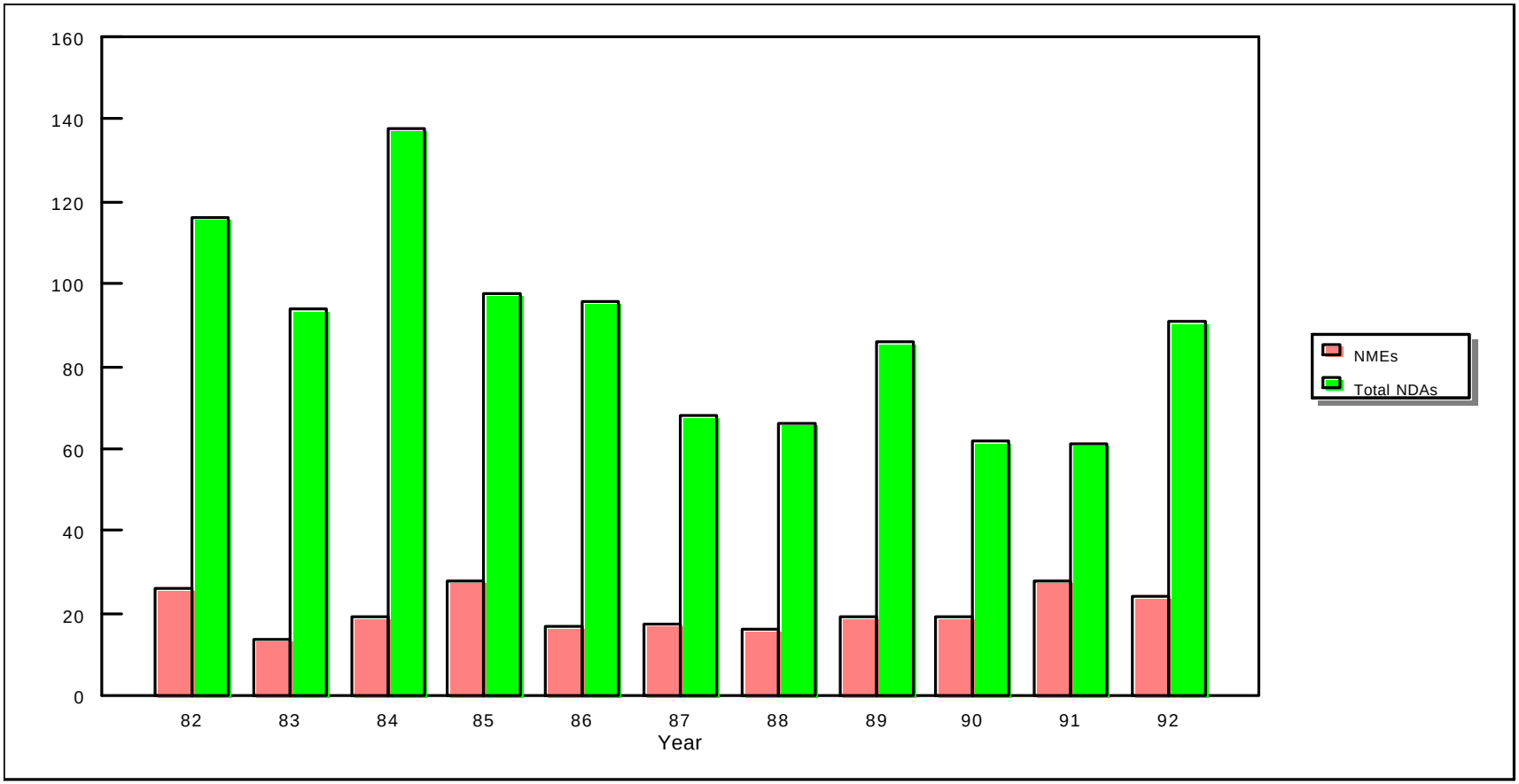

Figure 3-4. Number of Approved New Drug Applications (NDAs) and New Molecular Entities (NMEs): 1982-1992.

Source: U.S. FDA, 1992. *Office of Drug Evaluation: Statistical Report*. Rockville, MD: U.S. FDA.

approved drug (e.g., a new indication, revision of an approved indication, etc.). FDA approves approximately 60 percent of all NDAs and supplements received each year.[6] Figure 3-5 presents a breakdown of new drugs approved between 1987 and 1992 by major therapeutic category.

To prioritize NDAs for review, FDA classifies new drugs according to their potential therapeutic importance. Type A drugs represent drugs that might provide effective therapy or diagnosis for a disease that is not adequately treated or diagnosed by any marketed drug. Type B drugs have modest advantages over currently marketed drugs such as greater patient convenience and fewer side effects. Type C drugs have substantially equivalent therapeutic benefits as already marketed drugs. Approximately 22 percent of the new drugs approved by FDA between 1987 and 1992 were classified as either Type A or B, representing potentially significant therapeutic gains.[7]

3.1.2.2 Generic Drugs

When the patent on a prescription drug runs out, other manufacturers often enter the market with a generic version of the drug. To gain market approval, manufacturers of generic drugs must prove to FDA through an abbreviated NDA (ANDA) that their product is "bioequivalent" to a previously marketed drug—that is, that it contains identical active chemical ingredients and enters the bloodstream at the same rate and levels. Because demonstrating bioequivalence is generally much easier than proving the overall safety and effectiveness of a drug (FDA assumes that bioequivalence implies identical safety and effectiveness), generic drugs are generally approved much more quickly than new drugs.[8] Nonetheless, bioequivalence testing may take several years to complete. In the early 1990s, FDA approved an average of about 240

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[6] U.S. FDA, 1992. U.S. Food and Drug Administration. *Office of Drug Evaluation: Statistical Report.* Rockville, MD: U.S. FDA.

[7] U.S. FDA, 1992. *Op. cit.*

[8] Before 1984, manufacturers of generic drugs would often need to duplicate many of the original manufacturer's clinical tests to gain market approval. The 1984 Drug Price Competition and Patent Term Restoration Act (the 1984 Price Act) rescinded these strict controls for generics, stipulating that generic drug manufacturers need only demonstrate bioequivalence to a previously marketed drug. It is generally agreed that the 1984 Price Act has greatly facilitated the entry of generics into the pharmaceutical market.

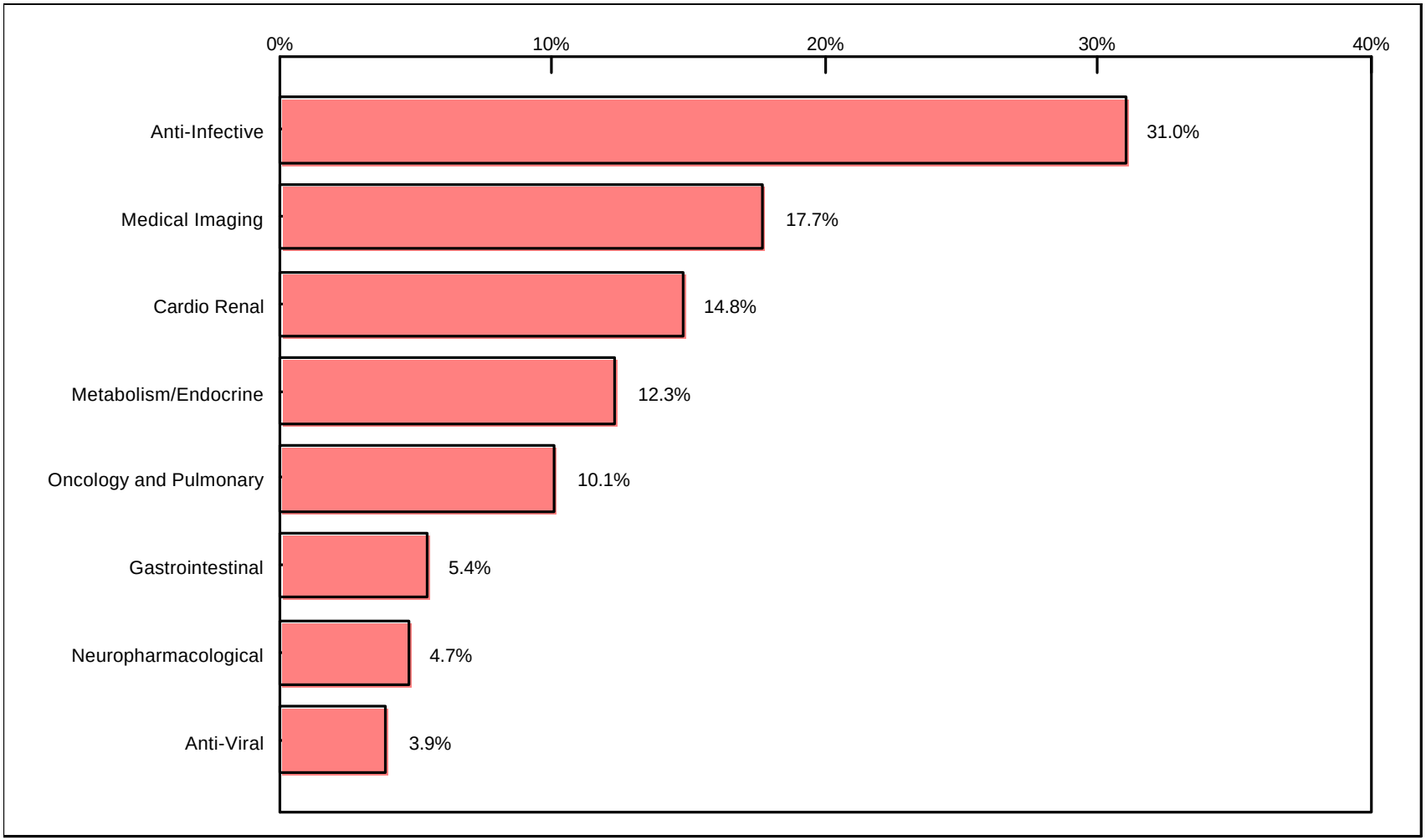

Figure 3-5. Approved NDAs by therapeutic category: 1987-1992.

Source: U.S. FDA, 1992. *Office of Drug Evaluation: Statistical Report*. Rockville, MD: U.S. FDA.

ANDAs per year.[9] An industry analyst places the current approval rate at 250 ANDAs per year.[10] The FDA web site reports 254 ANDAs approved in 1997.[11]

Since 1980, generic drugs have captured an increasing share of the prescription drug market. As shown in Figure 3-6, generic drugs accounted for 19.1 percent of prescription drug sales in 1991 (the most recent year for which sales data are available), almost double their market share in 1980. With rising health care costs, public and private insurers have put increasing pressure on health care providers to use less expensive generic drugs when available. According to industry analysts, the generic drug industry is poised to accumulate even greater market share over the next decade. Brand-named drugs representing annual sales of over $20 billion in 1992 were projected to lose patent protection between 1992 and 1996,[12] and PhRMA states that the generics share of the market (by number of prescriptions filled) rose from about 34 percent in 1991 to nearly 43 percent in 1995, suggesting that the predicted trend toward greater use of generics is occurring.[13]

3.1.2.3 OTC Drugs

FDA treats OTC drugs somewhat differently than other regulated pharmaceutical products. Before 1976, OTC drugs were not subject to the same NDA requirements. In 1976, however, FDA revised its OTC policy, calling for more rigorous regulation of the OTC market. In the same year, FDA embarked on an extensive review of all FDA approved ingredients of OTC drugs. FDA divided the previously broad grouping of OTC drugs into distinct therapeutic categories (e.g., sleeping aids, cough suppressants), each with their own monograph standard requiring specific labeling and dosages. In its review of OTC ingredients, FDA has removed many previously approved ingredients from the list of approved OTC ingredients. Once FDA's

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[9] Sherwood, Ted, 1993. U.S. Food and Drug Administration, Center for Drug Evaluation, Office of Generic Drugs. Telephone conversation. May 19, 1993.

[10] Moore, 1996. *Op. cit.*

[11] http://www.fda.gov/cder/da/da.htm

[12] NatWest, 1992. *Op. cit.*

[13] PhRMA, 1996. *Generic's Share of U.S. Market, 1984-1995. Op. cit.*

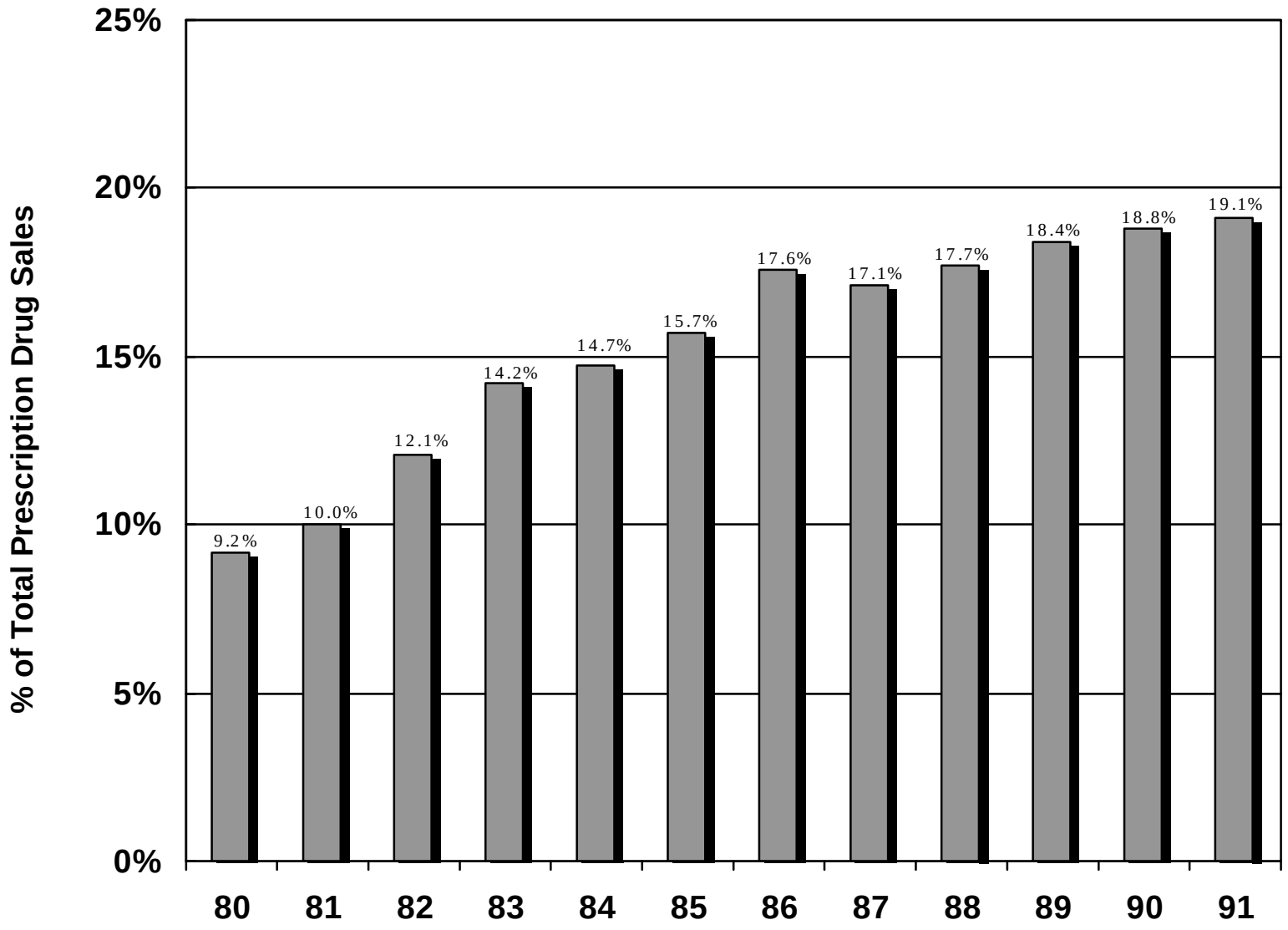

Figure 3-6. Generic prescription drug sales as a percentage of total prescription drug sales: 1980-1991.

Source: NatWest, 1992. *The U.S. Generic Drug Industry*. New York: NatWest.

review is complete, new OTC drugs that have not been monographed will have to submit safety and effectiveness data to FDA, much like that required in an NDA.

Like generics, OTC drugs are a growing segment of the overall pharmaceutical market. OTC trade organizations expect the OTC market share to continue to increase over the next decade as FDA increasingly grants OTC status to prescription drugs and as the move to control health care costs leads to greater use of less expensive OTC products. Within the OTC market itself, analgesics account for approximately 39 percent of total sales, cold medications 19 percent, and antacids 14 percent. Other OTC products such as antinausea drugs and cough medicines make up the remainder of the OTC market.

3.1.3 Manufacturing Processes

The pharmaceutical industry uses an array of complex batch-type processes and technologies in the manufacture of its products.[14] Rather than detailing specific processes and technologies, this section will describe the three main stages of pharmaceutical production: R&D, bulk drug manufacturing (via fermentation, extraction, and chemical synthesis), and finished pharmaceutical product formulation. These manufacturing processes roughly correspond to the EPA's subcategorization scheme described in Section Two (see Figure 3-7). As noted earlier, some pharmaceutical companies engage in all three stages of pharmaceutical manufacturing, while others focus on just one or two.

[14] For a detailed discussion of pharmaceutical manufacturing processes, please refer to EPA's 1982 and 1983 proposed and final development documents (U.S. EPA, 1982. U.S. Environmental Protection Agency. *Proposed Development Document for Effluent Limitations Guidelines and Standards for the Pharmaceutical Point Source Category*. Washington, DC: U.S. EPA; U.S. EPA, 1983. *Development Document for Effluent Guidelines, New Source Performance Standards, and Pretreatment Standards for the Pharmaceutical Manufacturing Point Source Category*. Washington, DC: U.S. EPA), as well as the 1995 and 1998 development documents for the current final rule. These sources are the basis for much of the discussion in Section 3.1.3.

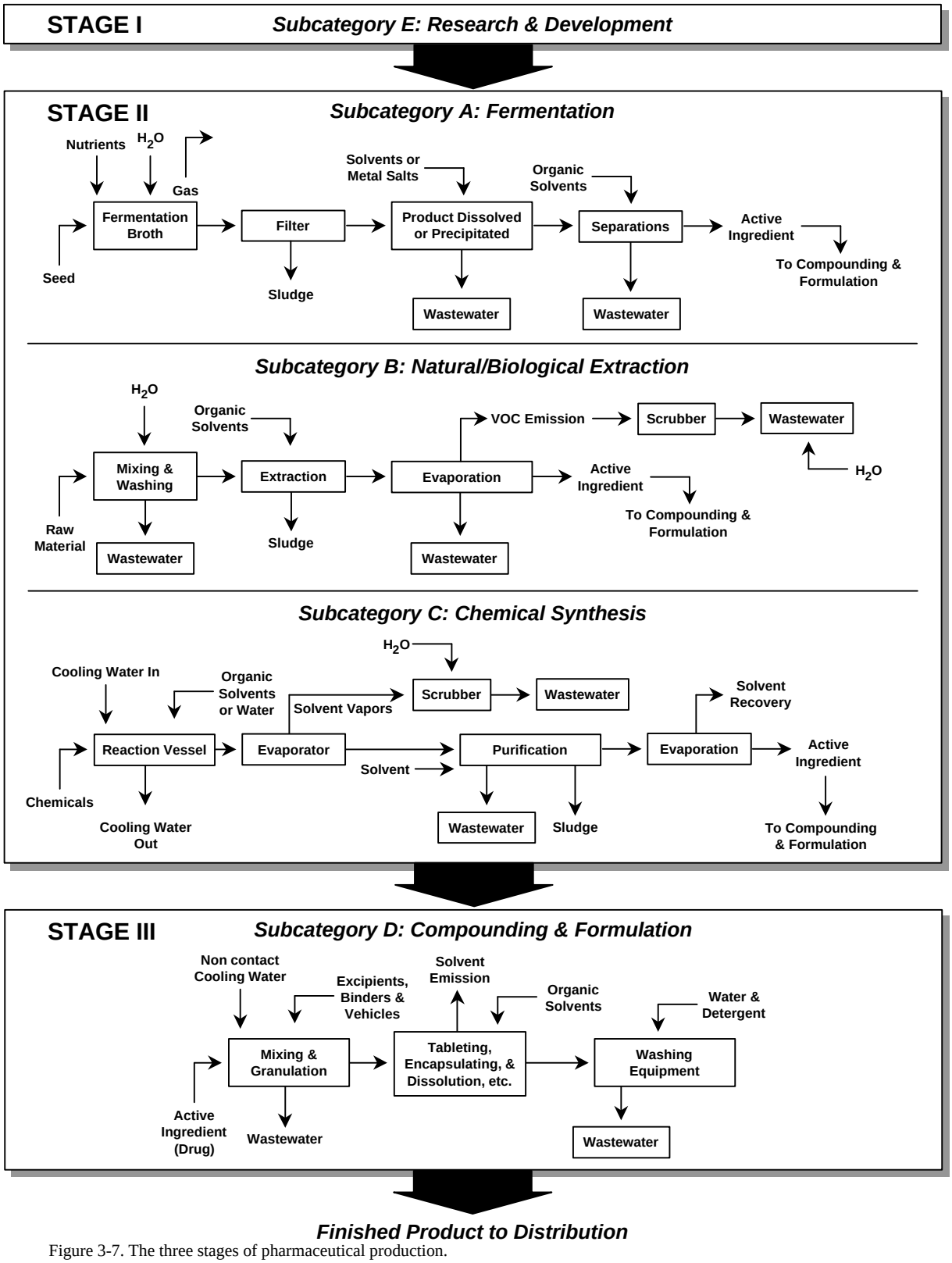

Figure 3-7. The three stages of pharmaceutical production.
Source: Adapted from EPA, 1992. *Pharmaceutical Manufacturing Industry: Revision of Effluent Guidelines.* Unpublished Status Briefing. Washington, DC: U.S. EPA.

3.1.3.1 Stage I—R&D

Stage I—R&D—is aimed at discovering, enhancing, and devising reliable manufacturing processes for drugs. As such, it serves the dual purpose of product development and manufacturing method development/manufacturing initiation. Corresponding to EPA's pharmaceutical industry subcategory E, pharmaceutical R&D encompasses several fields, including chemical, microbiological, and pharmacological research. A typical innovative pharmaceutical company employs specialized personnel with expertise in medicinal, organic, and analytical chemistry; microbiology; biochemistry; physiology; pharmacology; toxicology; chemical engineering; and pathology. The development of a new drug involves innumerable laboratory processes and years of experimental testing. The entire R&D process can take as long as 12 years to complete.[15]

3.1.3.2 Stage II—Bulk Drug Manufacturing

Stage II is aimed at converting organic and chemical substances into bulk active ingredients via one (or more) of three conversion processes—fermentation, extraction, or chemical synthesis. EPA's pharmaceutical industry (subcategories A, B, and C) correspond to these three conversion processes, respectively. The processes are defined as follows:[16]

- ***Fermentation (Subcategory A)***. Fermentation is the decomposition of complex substances (creating new substances) through the action of enzymes or ferments produced by microorganisms (usually bacteria, molds, or yeasts). The process begins in the laboratory with a carefully maintained population of a microbial strain. A few cells from this culture are grown into a dense suspension and then transferred to a seed tank designed for maximum cell growth. Material from the seed tank is then transferred to a vessel containing substances to be fermented. Following fermentation, the fermenter broth is filtered to remove solid residues. The filtrate is then processed to recover the desired product using solvent extraction, precipitation, and ion exchange or adsorption chromatography. Steroids, Vitamin B_{12}, and antibiotics are typically produced using a batch fermentation process.

[15] See Section 3.2.3 for a more detailed discussion of pharmaceutical R&D.

[16] Definitions adapted from U.S. EPA, 1991. *Guides to Pollution Prevention: The Pharmaceutical Industry*.

- ***Extraction (Subcategory B)***. Biological, or natural, extraction produces pharmaceuticals from natural material sources such as roots, leaves, and animal glands. Product recovery and purification processes include precipitation and solvent extraction. The amount of finished drug product is quite small compared with the volume of natural source material used. During each process step, the volume of material worked greatly diminishes to the point where final purification might occur on volumes of less than one-thousandth of the initial volume. Anticancer drugs, insulin, morphine, and hormones are examples of drugs manufactured using natural extraction processes.

- ***Chemical Synthesis (Subcategory C)***. Chemical synthesis takes place in a series of reaction, separation, and purification steps. Numerous types of chemical reactions, recovery processes, and chemicals are used to produce drugs through chemical synthesis. Chemicals used in chemical synthesis operations range widely and include organic and inorganic reactants and catalysts and a variety of solvents listed as priority pollutants by EPA. Most drugs today are produced by chemical synthesis. Examples include aspirin and acetaminophen.

A substance that is fermented, naturally extracted, or chemically synthesized might require no further processing to become a bulk active ingredient. Alternatively, additional chemical synthesis might be necessary before the desired active ingredient is formed. In either case, when large-scale production is undertaken, these conversion processes often involve discharges of process wastewater. Of the facilities included in the Section 308 Survey, 59 percent were engaged in one or more of the above processes.

3.1.3.3 Stage III—Finished Pharmaceutical Product Formulation

Stage III—formulation—refers to the combining of bulk active ingredients with other substances to produce dosage forms suitable for human or animal intake. Formulation corresponds to EPA subcategory D and can be defined as the preparation of dosage forms into tablets, capsules, liquids, parenterals (introduced internally other than by way of the intestines), and creams and ointments. Tablets account for 90 percent of all medications taken orally and are produced by blending active ingredients with fillers such as starch or sugar and binders such as corn starch. Hard and soft capsules consist of gelatin capsules that are filled with an active ingredient. Liquid dosage forms include syrups, elixirs, suspensions, and tinctures, all of which are prepared by mixing solutes with a selected solvent in a glass-lined or stainless steel vessel. Parenterals are injected into the body and are prepared as solutions, dry solids, suspensions, dry insoluble solids, and emulsions. Ointments and creams are semisolid dosage forms prepared for topical use. Like bulk

manufacturing, formulation (finished dosage form manufacturing) often involves discharges of process wastewater. Approximately 68 percent of the surveyed facilities had formulating operations.

Following formulation, finished drugs are distributed to hospitals, health maintenance organizations (HMOs), retail pharmacies, as well as directly to consumers.

3.2 FACILITY, OWNER COMPANY, AND PARENT COMPANY CHARACTERISTICS

This section presents facility, owner company, and parent company data for the pharmaceutical industry garnered from the U.S. Department of Commerce and the Section 308 Pharmaceutical Survey. The data cover numbers of establishments and employees, value of shipments, international trade, production costs, and baseline financial conditions. For the purpose of this EA, a facility is defined as an individual location where pharmaceutical products are manufactured and/or formulated. An owner company might control one or several individual facility locations. Owner companies might, in turn, be owned by a parent company. The U.S. Department of Commerce collects data only at the facility level; the Section 308 Pharmaceutical Survey collected financial data at all three levels. As discussed in Section Two, U.S. Department of Commerce data are more representative of the industry as a whole, whereas the survey data are more representative of the regulated community, since discharging facilities and their firms were the primary target of the survey. Each of the following sections begins by discussing U.S. Department of Commerce data, where available, and then follows with parallel survey data.[17]

[17] The following discussions use these sources: U.S. Bureau of the Census, 1997. *County Business Patterns:1995.* Washington, DC: U.S. Government Printing Office; U.S. Bureau of the Census, 1996. *County Business Patterns: 1994.* U.S. Government Printing Office.

Table 3-1

Number of Pharmaceutical Establishments by Employee Size:
SIC 283 Drugs

SIC Code	Total Number of Establishments		Number of Employees							
			1-19		20-99		100-249		>250	
	1990	1995	1990	1995	1990	1995	1990	1995	1990	1995
283 Drugs	1,343	1,529	623	765	416	419	141	165	154	180
2833 Medicinals and Botanicals	266	261	133	169	68	60	13	21	12	11
2834 Pharmaceutical Preparations	680	711	288	309	202	187	78	95	112	120
2835 Diagnostic Substances	161	251	60	99	56	89	26	32	19	31
2836 Biological Products, Except Diagnostics	220	284	97	167	88	82	24	17	11	18

Sources: U.S. Bureau of the Census, 1997. *County Business Patterns: 1995.* Washington, DC: U.S. Government Printing Office; U.S. Bureau of the Census, 1993. *County Business Patterns: 1990.* Washington, DC: U.S. Government Printing Office.

3.2.1 Number of Establishments and Employees

3.2.1.1 U.S. Department of Commerce Data

In 1990, the U.S. Department of Commerce classified some 1,343 establishments (i.e., facilities) involved in producing SIC 283 drugs. In 1995, that number grew to 1,529 (see Table 3-1).[18] Approximately half of these establishments (51 to 47 percent in 1990 and 1995, respectively) were producing SIC 2834 drugs (pharmaceutical preparations), with the remaining establishments divided among SICs 2833, 2835, and 2836. Between 1990 and 1995, the number of establishments in SICs 2835 and 2836 (diagnostic substances; biological products, except diagnostics) grew faster than the number of establishments in SICs 2833 and 2834 (medicinals and botanicals; pharmaceutical preparations).

Together, SIC 283 pharmaceutical establishments employed 218,000 people in 1995,[19] an increase of 11 percent over 1989 employment levels (see Table 3-2). In contrast to the substantial growth that occurred in the 1980s, however, pharmaceutical employment remained relatively steady between 1989 and 1992, but by 1995 has increased somewhat over 1992 levels. Due to cost pressures arising from the advent of price discounting, weak foreign economies, increased use of generic and OTC drugs, and the previous anticipation of increased government controls under health care reform, many pharmaceutical firms underwent significant restructuring in the early to mid 1990s—including substantial job cuts. These trends disproportionately affected establishments in SIC 2834 (pharmaceutical preparations), while those in SIC 2835 (diagnostic substances) fared significantly better than other SIC 283 industries. Although employment remained heavily concentrated in SIC 2834, this sector's share of total industry employment dropped from 80 percent to 70 percent between 1990 and 1991. With continued investment in R&D to discover and bring to

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[18] In reality, there are probably more establishments manufacturing pharmaceuticals than are indicated by U.S. Department of Commerce data. Because U.S. Department of Commerce classifies facilities by their primary line of business, the four pharmaceutical SIC codes do not capture facilities that manufacture pharmaceuticals but whose primary business is classified in some other SIC code.

[19] PhRMA puts industry employment much higher than that for equivalent years shown in Table 3-2—213,651 in 1992 and 208,460 in 1994 (PhRMA, 1996. *Summary of Industry Employment Statistics from Various Sources.* Document Number 5090. Pharmaceutical Research and Manufacturers of America). PhRMA's employment data are based on the association's annual members survey. Because PhRMA's members include large corporations that also engage in activities outside the pharmaceutical industry, however, PhRMA's data may overstate employment in this industry.

Table 3-2

Total Number of Employees and Production Workers:
SIC 283 Drugs
(1989-1995)

SIC Code		1989	1990	1991	1992	1993	1994	1995
Total Employment								
283	Drugs	196,000	194,000	203,000	194,000	218,000	205,000	218,000
2833	Medicinals and Botanicals	11,400	11,700	13,700	13,100	13,000	12,900	14,300
2834	Pharmaceutical Preparations	142,000	155,000	142,000	123,000	128,000	133,000	142,000
2835	Diagnostic Substances	16,100	16,000	33,500	39,900	39,300	39,100	39,800
2836	Biological Products, Except Diagnostics	14,500	14,300	13,300	18,500	19,000	19,800	21,100
Production Workers								
283	Drugs	82,800	86,800	90,100	92,700	94,600	102,000	113,000
2833	Medicinals and Botanicals	6,600	6,900	7,800	7,500	7,700	7,500	7,700
2834	Pharmaceutical Preparations	62,400	65,700	64,600	62,400	62,800	68,000	78,300
2835	Diagnostic Substances	6,800	7,000	10,800	14,700	14,900	16,100	15,600
2836	Biological Products, Except Diagnostics	7,000	7,200	6,900	8,100	9,200	9,900	11,000

Source: U.S. Department of Commerce, 1994. *U.S. Industrial Outlook: 1994.* Washington, DC: U.S. Government Printing Office; U.S. Bureau of the Census, 1997. *Statistical Abstract of the United States: 1997*. Washington, DC.

market new drugs, more experience in competing with generics and OTCs, improving economies, and a leveling of concern about health care reform, pharmaceutical industry employment (including SIC 2834 employment) has begun to grow again and is expected to continue growing for the next few years, albeit at a slower pace than that seen in the 1980s, as is evidenced by the general growth in employment between 1992 and 1995. Throughout the 1980s and 1990s, the proportion of the industry's workforce involved in production has remained about the same: between 45 and 46 percent.

Smaller establishments (less than 100 employees) dominate the pharmaceutical industry, accounting for 77 percent of all establishments in SIC 283 in both 1990 and 1995. In fact, about half of all establishments (46 percent in 1990, 50 percent in 1995) employ fewer than 20 people. The industry, however, does have an unusually high percentage of establishments with more than 250 employees (11 and 12 percent in 1990 and 1995, respectively) when compared to the manufacturing sector overall, in which only 4 percent of establishments have more than 250 employees. As discussed in Section 3.3, the presence of an unusually high percentage of large facilities and firms in the industry can be attributed to the enormous financial commitment necessary to develop and market new products and the existence of economies of scale in pharmaceutical manufacturing. With the pharmaceutical industry firm restructuring that occurred in the early 1990s—which included a number of company mergers/consolidations (especially among larger firms) and sales of R&D or other divisions (especially among smaller firms) as well as job cuts—many large firms became even larger, while many smaller firms became even smaller.

3.2.1.2 Section 308 Pharmaceutical Survey Data

EPA estimates that approximately 286 of the industry's 1,343 establishments are either direct or indirect dischargers and therefore potentially would be affected by revised effluent regulations. The Section 308 Survey censused or sampled 244 of these establishments to represent the 286 facilities. Of the 286 facilities, 73 percent are owned by other companies. Only 27 percent of the surveyed facilities indicated that they were independently owned. In 1990, 69 parent companies owned 56 percent of the surveyed establishments.

Employment data were collected at the facility level only (see Table 3-3). According to the survey data, only 6 percent of all establishments had fewer than 20 employees. This pattern is in contrast to U.S.

Table 3-3

Surveyed Facilities by Number of Employees

Number of Employees	Number of Facilities	Percentage of All Facilities
1-19	18	6%
20-99	57	20%
100-249	55	19%
250-500	54	19%
501-999	57	20%
>1000	45	16%
Total	286	100%

Source: Section 308 Pharmaceutical Survey.

Department of Commerce data, which indicate that roughly half of all pharmaceutical establishments employ fewer than 20 employees. Conversely, where U.S. Department of Commerce reports that only 11 percent of pharmaceutical establishments have more than 250 employees, nearly 55 percent of the surveyed establishments reported employment of over 250 people. The fact that surveyed establishments include a much higher proportion of large facilities than the pharmaceutical industry as a whole makes sense, since we would expect most dischargers to be major bulk drug manufacturers or vertically integrated pharmaceutical firms that engage in a great deal of large-scale manufacturing (typically at a large facility) rather than exclusively R&D or marketing firms (typically smaller facilities or firms). In the surveyed facilities, approximately 70 percent of manufacturing employment is concentrated in pharmaceutical manufacturing. Over 50 percent of the surveyed facilities reported no employment in nonpharmaceutical-related activities.

3.2.2 Value of Shipments

3.2.2.1 U.S. Department of Commerce Data

According to the U.S. Department of Commerce, drug industry shipments increased about 6 percent in 1993 to $69 billion, an estimate that includes all products shipped by establishments classified in SICs 2833 through 2836. Shipments of drug products alone totaled about $58.4 billion in 1993. In current dollars, drug industry shipments grew at a rate of 9 to 12 percent between 1987 and 1991; since 1991, these shipments have grown at a slower pace, between 2.1 and 7.4 percent annually. In real terms, growth in most years has averaged about 2 percent annually. Table 3-4 lists total industry shipments ($1990) and drug product shipments between 1987 and 1994. The data indicate that the industry performed well despite the recession in the early 1990s and the various cost pressures and trends described above. Sales data from PhRMA (based on PhRMA's annual survey of its members) generally agree with these Department of Commerce data and trends. PhRMA data suggest that industry performance has continued to be strong, with estimated 3.7 percent and 8.8 percent increases in sales in 1995 and 1996, respectively.[20]

[20] PhRMA, 1996. *Growth in Domestic U.S. Sales and Sales Abroad, Ethical Pharmaceuticals, PhRMA Member Companies, 1970-1996.* Document Number 5060. Pharmaceutical Research and Manufacturers of America.

Table 3-4

Value of Shipments: SIC 283 Drugs
(millions of 1990 dollars)

Code		1987	1988	1989	1990	1991	1992	1993	1994	1995
Industry Shipments†										
283	Drugs	$42,168	$46,054	$50,342	$56,715	$63,468	$64,335	$64,454	$6,6329	$69,965
2833	Medicinals and Botanicals	$3,598	$4,345	$4,872	$5,194	$6,581	$6,193	$5,381	$5,331	$6,088
2834	Pharmaceutical Preparations	$34,469	$37,509	$41,029	$46,646	$49,426	$45,777	$48,379	$49,108	$50,121
2835	Diagnostic Substances	$2,368	$2,367	$2,383	$2,599	$4,952	$6,507	$6,233	$7,243	$8,370
2836	Biological Products, Except Diagnostics	$1,733	$1,832	$2,058	$2,276	$2,510	$3,789	$4,462	$4,646	$5,386
Product Shipments††										
283	Drugs	$37,894	$41,390	$44,891	$47,831	$50,791	$57,693	$58,085	$59,282	$61,775
2833	Medicinals and Botanicals	$4,537	$5,181	$5,528	$5,789	$6,507	$6,645	$6,128	$5,926	$6,339
2834	Pharmaceutical Preparations	$28,579	$30,944	$33,531	$35,280	$36,630	$40,885	$41,334	$42,075	$42,848
2835	Diagnostic Substances	$2,882	$3,207	$3,558	$4,234	$4,869	$5,880	$5,859	$6,282	$7,154
2836	Biological Products, Except Diagnostics	$1,896	$2,058	$2,276	$2,529	$2,784	$4,282	$4,763	$5,001	$5,434

† Value of all products and services sold by establishments in the pharmaceutical industry.
†† Value of products classified in the pharmaceutical industry produced by all industries.

Source: U.S. Bureau of the Census, 1997. *Statistical Abstract of the United States: 1997*. Washington, DC: U.S. Government Printing Office; U.S. Department of Commerce, 1994. *U.S. Industrial Outlook: 1994*. Washington, DC: U.S. Government Printing Office.

Table 3-5

Value of Shipments by Employee Size of Establishment: SIC 283
(millions of 1990 dollars)

Employee Size	Number of Establishments		Number of Employees		Value of Shipments		Value of Shipments Per Employee	
	1987	1992	1987	1992	1987	1992	1987	1992
<20 employees	696	702	4,800	5,000	$813	$1,088	$0.17	$0.22
20-99 employees	390	421	17,200	19,600	$2,815	$4,440	$0.16	$0.23
99-500 employees	200	219	43,200	55,600	$13,034	$21,254	$0.30	$0.38
>500 employees	70	80	104,700	113,900	$25,505	$37,436	$0.30	$0.33

Source: U.S. Department of Commerce, 1995. *U.S. Census of Manufactures: 1992.* MC92-S-2. Washington, DC: U.S. Government Printing Office; U.S. Department of Commerce, 1991. *U.S. Census of Manufactures: 1987.* MC87-S-6 (CD-ROM). Washington, DC: U.S. Government Printing Office.

tend to ship a greater proportion of the relatively expensive finished, branded pharmaceutical products than do smaller establishments, which are more likely to ship bulk, generic, and OTC pharmaceutical products.

The data in Table 3-5 also show that shipments per employee ($1990) generally increase across size classes, indicating the possible presence of economies of scale (see Section 3.3.1). Although the number of employees increased in all size classes between 1987 and 1992, the value of shipments increased even more—so that the value of shipments per employee increased substantially between 1987 and 1992. This suggests that employee productivity rose during this time.

A large majority of industry shipments is attributed to SIC 2834 Pharmaceutical Preparations, which in 1995 had sales totaling $45 billion (see Table 3-4). Like this sector's share of total pharmaceutical employment (see Section 3.2.1.1), SIC 2834 establishments' share of industry shipments has declined somewhat in recent years—from about 80 percent in the late 1980s to about 74 percent in the early 1990s. The U.S. Department of Commerce further breaks down SIC 2834 shipments into five-digit SIC codes representing individual therapeutic categories. Table 3-6 presents value of shipments data for nine therapeutic categories within SIC 2834. As can be seen in 1996, 77 percent of SIC 2834 shipments are for prescription drugs, 21 percent are for OTC drugs, and 2 percent are for bulk shipments. Because prescription products typically cost more per unit than OTC and bulk drugs, shipment data for these three product groups would be somewhat closer if reported by shipment volume rather than shipment value. OTC drugs account for the greatest portion of shipments in SICs 28349, pharmaceutical preparations for veterinary use; 28346, pharmaceutical preparations acting on the skin; and 28344, pharmaceutical preparations acting on the respiratory system.

3.2.2.2 Section 308 Survey Data

The Section 308 Survey collected data on pharmaceutical and nonpharmaceutical revenues at the facility, owner company, and parent company levels.[21] Only 212 facilities reported revenues for all 3 years

[21] Unless otherwise noted, all revenue data is reported in 1990 dollars.

Table 3-6

Value of Product Shipments by Prescription/Nonprescription: SIC 2834 Pharmaceutical Preparations (millions of 1990 dollars)

SIC Code	Product Description	1993				1994			
		Total	Prescription	Nonpre-scription	Bulk	Total	Prescription	Nonpre-scription	Bulk
28341	Pharmaceutical preparations affecting neoplasms, endocrine system, and metabolic diseases, for human use.	$3,465	$3,350	$28	$87	$3,616	$3,541	$29	$46
28342	Pharmaceutical preparations acting on the central nervous system and the sense organs, for human use.	$8,097	$5,991	$2,051	$55	$7,932	$6,046	$1,828	$58
28343	Pharmaceutical preparation acting on the cardiovascular system, for human use.	$4,747	$4,560	$34	$154	$4,854	$4,680	$11	$162
28344	Pharmaceutical preparations acting on the respiratory system, for human use.	$4,998	$2,827	$2,140	$30	$4,966	$3,037	$1,890	$38
28345	Pharmaceutical preparation acting on the digestive or the genito-urinary systems, for human use.	$7,252	$5,866	$1,357	$29	$7,724	$6,446	$1,235	$43
28346	Pharmaceutical preparations acting on the skin, for human use.	$1,796	$579	$1,209	$7	$1,942	$552	$1,378	$11
28347	Vitamin, nutrient, and hemantic preparations, for human use.	$3,229	$1,164	$1,728	$337	$3,857	$1,484	$1,969	$404
28348	Pharmaceutical preparations affecting parasitic and infective diseases, for human use.	$6,561	$5,795	$665	$102	$7,165	$6,414	$608	$143
28349	Pharmaceutical preparations for veterinary use.	$1,226	$444	$710	$73	$1,151	$398	$705	$47
Total for SIC 2834		$41,371	$30,576	$9,922	$874	$43,205	$32,560	$9,652	$952
% of Total for SIC 2834		100%	74%	24%	2%	100%	75%	22%	2%

Table 3-6 (continued)

SIC Code	Product Description	1995				1996			
		Total	Prescription	Non prescription	Bulk	Total	Prescription	Non prescription	Bulk
28341	Pharmaceutical preparations affecting neoplasms, endocrine system, and metabolic diseases, for human use.	$3,526	$3,444	$57	$24	$4,021	$3,946	$40	$34
28342	Pharmaceutical preparations acting on the central nervous system and the sense organs, for human use.	$7,982	$6,039	$1,862	$81	$8,594	$6,722	$1,808	$65
28343	Pharmaceutical preparation acting on the cardiovascular system, for human use.	$5,180	$5,046	$11	$122	$5,865	$5,736	$19	$110
28344	Pharmaceutical preparations acting on the respiratory system, for human use.	$4,495	$2,832	$1,614	$48	$4,361	$2,764	$1,518	$78
28345	Pharmaceutical preparation acting on the digestive or the genito-urinary systems, for human use.	$7,433	$6,256	$1,149	$29	$7,243	$6,146	$1,060	$38
28346	Pharmaceutical preparations acting on the skin, for human use.	$1,878	$578	$1,280	$20	$1,746	$615	$1,120	$13
28347	Vitamin, nutrient, and hemantic preparations, for human use.	$4,162	$1,504	$2,236	$422	$4,558	$1,478	$2,626	$453
28348	Pharmaceutical preparations affecting parasitic and infective diseases, for human use.	$6,224	$5,462	$594	$168	$6,078	$5,438	$520	$120
28349	Pharmaceutical preparations for veterinary use.	$1,388	$684	$642	$63	$1,474	$837	$597	$40
Total for SIC 2834		$42,267	$31,845	$9,445	$977	$43,939	$33,681	$9,309	$950
% of Total for SIC 2834		100%	76%	22%	2%	100%	77%	21%	2%

Prescription: A drug product that, by federal law, is available only by prescription by a licensed physician.
Nonprescription: A drug product that is sold over the counter, whether advertised or otherwise promoted to the professions or the general public.
Bulk: Represents the value of dosage forms shipped in bulk to other plants of the same company or other companies.
Source: U.S. Department of Commerce, 1996, 1995, 1994. *Current Industrial Reports: Pharmaceutical Preparations, Except Biologicals*. MA28G(96)-1, MA28G(95)-1, MA28G(94)-1. Washington, DC: U.S.Government Printing Office.

Table 3-7

Facility, Owner Company, and Parent Company Revenues (billions of 1990 dollars)

Production Cost Category	1988		1989		1990	
	Total	Average	Total	Average	Total	Average
Facilities (n = 212)						
Revenues from sales of pharmaceutical products (domestic and international)	$13.4	$0.06	$14.6	$0.07	$17.0	$0.08
Nonpharmaceutical sales	$3.4	$0.02	$4.0	$0.02	$4.2	$0.02
Total revenues*	$16.8	$0.08	$18.6	$0.09	$21.2	$0.10
Owner Companies (n = 157)						
Revenues from sales of pharmaceutical products (domestic and international)	$42.6	$0.3	$44.4	$0.3	$48.8	$0.3
Nonpharmaceutical sales	$42.6	$0.3	$48.2	$0.3	$48.9	$0.3
Total revenues*	$86.9	$0.6	$94.4	$0.6	$99.8	$0.6
Parent Companies (n = 68)						
Revenues from sales of pharmaceutical products (domestic and international)	$73.3	$1.1	$80.6	$1.2	$80.7	$1.2
Nonpharmaceutical sales	$213.7	$3.1	$215.1	$3.2	$218.7	$3.2
Total revenues*	$292.3	$4.3	$295.7	$4.3	$305.2	$4.5

*Pharmaceutical revenues and nonpharmaceutical revenues might not add to total revenues because of inconsistencies in survey reporting.
Source: Section 308 Pharmaceutical Survey.

Table 3-8

Distribution of Surveyed Facilities by Value of Shipments: 1990

Value of Shipments (Millions of Dollars)	Pharmaceutical Shipments		Nonpharmaceutical Shipments		Total Shipments	
	Number of Facilities	Percentage of Facilities	Number of Facilities	Percentage of Facilities	Number of Facilities	Percentage of Facilities
0	3	1%	132	62%	3	1%
>0-1	2	1%	15	7%	11	5%
>1-5	29	14%	9	4%	17	8%
>5-25	64	30%	25	12%	65	31%
>25-100	50	24%	21	10%	62	29%
>100-250	31	15%	8	4%	36	17%
>250	15	7%	2	1%	18	8%

Source: Section 308 Pharmaceutical Survey.

surveyed.[22] As shown in Table 3-7, these 212 facilities generated $21.2 billion in revenues in 1990, an average of approximately $100 million per facility. Pharmaceutical revenues accounted for over 80 percent of total revenues. Table 3-8 shows the distribution of facilities by pharmaceutical, nonpharmaceutical, and total revenues. Over 62 percent of the facilities reported having no nonpharmaceutical revenues at all.

Company-level pharmaceutical revenues in the sample totaled $42.6 billion in 1988, $44.4 billion in 1989, and $48.8 billion in 1990 (see Table 3-7).[23] Total company-level revenues in the sample (including nonpharmaceutical revenues) totaled $86.9 billion in 1988, $94.4 billion in 1989, and $99.8 billion in 1990. Average revenues remained essentially flat over the period at approximately $600 million per owner company. Owner companies in the sample generated close to 50 percent of total revenues from pharmaceuticals.[24]

Parent company pharmaceutical revenues in the sample totaled $73.3 billion in 1988, $80.6 billion in 1989, and $80.7 billion in 1990. Total revenues reported by parent companies included in the survey came to $292.3 billion in 1988, $295.7 billion in 1989, and $305.2 billion in 1990. In 1990, parent companies generated 27 percent of their revenues from the sale of pharmaceuticals.

Table 3-9 shows the distribution of surveyed owner companies and parent companies by total revenues. Approximately one-third of the owner companies reported revenues of less than $25 million, one-third reported between $25 and $200 million, 21 percent between $200 million and $1 billion, and the remaining 13 percent over $1 billion. Approximately one-third of the parent companies sampled reported revenues of less than $250 million, 16 percent between $250 million and $1 billion, 35 percent between $1 billion and $10 billion, and 16 percent over $10 billion.

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[22] It has not been determined why so many of the surveyed facilities failed to report revenues for all 3 years surveyed. This lack of reporting may be caused by change of ownership.

[23] Approximately 42 percent of the owner companies surveyed derive 100 percent of their revenues from pharmaceutical sales.

[24] Company-level revenues from the survey and U.S. Department of Commerce are not directly compared because foreign revenues are treated differently.

Table 3-9

Number of Surveyed Owner Companies and Parent Companies by Total Revenues: 1990 (millions of 1990 dollars)

Owner Companies		Parent Companies	
Total Revenues	**Number of Companies**	**Total Revenues**	**Number of Companies**
$0-$25	50	$0-$250	23
≥$25-$200	50	≥$250-$1,000	11
≥$200-$1,000	33	≥$1,000-$10,000	24
≥$1,000	24	≥$10,000	10

Source: Section 308 Pharmaceutical Survey.

3.2.3 Production Costs

This section presents R&D, manufacturing, and marketing cost data for the pharmaceutical industry.[25] Production costs are broken down in this way because these cost categories play very different roles in industry performance—and in individual companies' decisions to engage in these activities. (Recall that the pharmaceutical industry includes many companies that focus on one or two of these areas, while many large companies engage in all three.) R&D and promotional costs, in particular, play a unique and critical role in realizing long-term gains in the pharmaceutical industry.

3.2.3.1 Research and Development

The cost of researching, developing, and obtaining market approval for a new drug is a significant component of total production costs. According to the U.S. Department of Commerce, the pharmaceutical industry spent approximately $11 billion in 1992 on R&D.[26] The industry spent $12.6 billion—14.5 percent more—in 1993.[27] These expenditures amounted to more than 16 percent of sales, one of the highest investment levels in any U.S. industry, and double the level invested in other high-technology industries. PhRMA estimates that its members spent about $13 billion to $14 billion on R&D in 1994 and 1995 and projects spending $15.8 billion in 1996—an all-time high representing about 19 percent of sales.[28] FDA estimates that 9 percent of all U.S. industrial R&D is in pharmaceuticals.[29]

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[25] Unless otherwise noted, all cost data are presented in 1990 dollars.

[26] U.S. Department of Commerce, 1993. *Op. cit.*

[27] U.S. Department of Commerce, 1994. *Op. cit.*

[28] PhRMA, 1996. R&D as a Percent of U.S. Sales, *Ethical Pharmaceuticals, PhRMA Member Companies, 1970-1996.* Document Number 5070. (Also Document Numbers 8013, 8019, and 8021.) Pharmaceutical Research and Manufacturers of America.

[29] FDA, 1990. U.S. Food and Drug Administration, Office of Drug Evaluation. *Overview of the Competitiveness of the U.S. Pharmaceutical Industry*. Presentation to the Council on Competitiveness. Rockville, MD: U.S. FDA.

Table 3-10

Cost of Pharmaceutical Production in Surveyed Population
(billions of 1990 dollars)

Production Cost Category	1988		1989		1990	
	Total	Average	Total	Average	Total	Average
Facility Level (n = 204)						
Cost of pharmaceutical products	$6.1	$0.03	$6.3	$0.03	$6.4	$0.03
Cost of nonpharmaceutical products	$1.3	$0.01	$3.1	$0.02	$3.2	$0.02
Total cost of goods sold	$7.4	$0.04	$9.4	$0.05	$9.6	$0.05
Company Level (n = 98)						
Cost of pharmaceutical products	$19.7	$0.2	$20.0	$0.2	$21.3	$0.2
Cost of nonpharmaceutical products	$39.0	$0.4	$43.0	$0.4	$42.5	$0.4
Total cost of goods sold	$58.7	$0.6	$63.0	$0.6	$63.8	$0.7
Total operating cost (not including cost of goods)	$35.6	$0.4	$40.0	$0.4	$40.0	$0.4
Research and development expenditures	$9.8	$0.1	$10.3	$0.1	$10.9	$0.1
Parent Company Level (n = 63)						
Cost of pharmaceutical products	$25.3	$0.4	$27.6	$0.4	$29.7	$0.5
Cost of nonpharmaceutical products	$123.8	$2.0	$134.8	$2.1	$145.6	$2.3
Total cost of goods sold	$149.1	$2.4	$162.4	$2.6	$177.3	$2.8
Total operating cost (not including cost of goods)	$67.7	$1.1	$77.1	$1.2	$86.0	$1.4
Research and development expenditures	$14.3	$0.2	$15.6	$0.2	$17.4	$0.3

Source: Section 308 Pharmaceutical Survey.

Data on R&D and other production costs in the pharmaceutical industry are also available from the Section 308 Pharmaceutical Survey. Table 3-10 presents cost data at the facility, owner company, and parent company levels for the sampled entities. Costs are broken down into the cost of pharmaceutical products and nonpharmaceutical products (including the cost of labor, capital, materials, and overhead), total operating expenditures (e.g., energy, depreciation), and R&D. In 1990, R&D costs among the surveyed firms amounted to $10.9 billion at the company level (an average of $100 million per owner company) and $17.4 billion at the parent company level (an average of $300 million). R&D costs averaged approximately 20 percent of the cost of goods sold over the 3 years reported in both owner and parent companies. The reported expenditures include nonpharmaceutical R&D expenditures as well. R&D cost data were not available at the facility level.

The research required to discover and develop NMEs is central to pharmaceutical R&D, because manufacturers of generics and chemically similar products build on the knowledge produced in the course of developing NMEs. NMEs are discovered either through screening existing compounds or designing new molecules. Once discovered, NMEs undergo rigorous preclinical testing in laboratories and animals and then clinical testing in humans to establish the compounds' safety and effectiveness (see Section 3.1.2.1). Further clinical studies might be conducted following market approval.

The primary component of R&D cost is labor. Pharmaceutical R&D draws on the expertise of a diverse array of biological, chemical, and physical scientists to discover NMEs with potential therapeutic benefits. Also of importance in pharmaceutical R&D is the opportunity cost of capital, which can be quite high given the risk and time involved. By some estimates, for every 9,999 compounds on which research is conducted, only one drug product is introduced to the market. A typical pharmaceutical company will require 9 to 12 years to bring an NME to market.[30] PhRMA's estimates are slightly different (1 of 5,000 compounds reach the market, with an average "lab to medicine chest" time of 12 to 15 years), but also indicate the magnitude of the risk and time involved in R&D.[31]

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[30] U.S. Congress, Office of Technology Assessment (OTA), 1993. *Pharmaceutical R&D: Costs, Risks, and Rewards.* Washington, DC: U.S. Government Printing Office.

[31] Moore, 1996. *Op. cit.*

Tuft's Center for the Study of Drug Research, a research institute specializing in the pharmaceutical industry, estimated that it costs an average of $231 million ($1990) to bring an NME to market. Approximately half of this total is the cost of capital.[32] In a study of the costs of pharmaceutical R&D, the Office of Technology Assessment (OTA) estimated that the aftertax R&D cash outlay for each NME that reached the market in the 1980s was about $65 million ($1990). The full aftertax cost of these outlays, compounded over 12 years to the day of market approval, was approximately $194 million ($1990).[33] More recently, an industry analyst cited estimates of $200 million to $500 million.[34] These cost estimates include R&D expenditures for unsuccessful as well as successful product development efforts, according to OTA. Moreover, an industry analyst noted that even of those compounds that do make it to market, only two or three out of every ten are profitable enough to recover their R&D costs; thus, high-sales drugs must pay for their own R&D costs, the R&D costs of lower sales drugs, and the R&D costs of drugs that never make it to market.[35]

OTA points out that the cost of pharmaceutical R&D is highly sensitive to changes in science and technology and in the regulatory environment, both of which are continuously evolving. Consequently, OTA warns that one cannot predict future R&D costs from current estimates, which are based on R&D costs for drugs that went into development more than 10 years ago. Nevertheless, some evidence, including the industry data noted above, suggests that pharmaceutical R&D is becoming more expensive over time as firms devote greater resources to hiring scientists, investing in new technology, and submitting their products to more extensive preclinical and clinical testing.

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[32] DiMasi, J.A., Hansen, R.W., Grabowski, H.G., et al., 1991. The Cost of Innovation in the Pharmaceutical Industry. *Journal of Health Economics* 10:107-142.

[33] OTA, 1993. *Op. cit.*

[34] Moore, 1996. *Op. cit.*

[35] *Ibid.*

3.2.3.2 Manufacturing Costs

Data on manufacturing (product and operating) costs from the Section 308 Pharmaceutical Survey are presented in Table 3-10. Product and operating costs rose from 1988 to 1990 in real terms ($1990) at the facility, owner company, and parent company levels. Excluding R&D expenditures, the total cost of production rose from $7.4 billion to $9.6 billion at the facility level, from $58.7 billion to $63.8 billion at the owner company level, and from $149.1 billion to $177.3 billion at the parent company level. The cost of pharmaceutical production as a percentage of the total cost of goods sold was approximately 67 percent at the facility level, 33 percent at the owner company level, and 17 percent at the parent company level in 1990.

3.2.3.3 Marketing

Promotional expenditures amount to approximately 22 percent of the industry's revenues.[36] Promotional expenditures tend to decline as a percentage of total sales over the life of the drug. For example, OTA estimates that in the second year following market approval, promotional expenditures account for 50 percent of sales. By the product's tenth year, however, promotional expenditures will have declined to only 6.5 percent of sales.[37]

Many view these high promotional expenditures as evidence that the industry does not compete on the basis of price and instead devotes excessive resources to product differentiation through advertising. Others contend that price should not be the only (or even the main) basis for competition in the therapeutic arena—that because good patient care dictates matching patient characteristics with drug features, promotional expenditures serve a useful and appropriate function in educating physicians about proper drug uses (i.e., through differentiating products by clinical as well as cost features). In addition, these analysts argue, high promotional expenditures help increase competition by allowing new competitors to enter specific drug markets. These issues are discussed further in Sections 3.3.1 and 3.3.3.

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[36] Day, Kathleen, 1993. Putting a Price on a Pill: Drug Firms Weigh New Intangibles in Setting Costs. *The Washington Post.* March 21,1993.

[37] OTA, 1993. *Op. cit.*

3.2.4 International Trade

3.2.4.1 U.S. Department of Commerce Data

With U.S. manufacturers accounting for nearly half of the major pharmaceuticals marketed worldwide, the U.S. pharmaceutical industry has consistently maintained a positive balance of trade in international markets. In 1991, the industry's trade surplus totaled $919 million; exports totaled $5.7 billion compared to $4.8 billion in imports. The U.S. Department of Commerce estimates that the industry's trade surplus declined to $755 million in 1992, rose to $1,059 million in 1993, and declined again to $526 million in 1994 due to increasing international competition, price controls, illegal use of patents and copyrights, and foreign regulations on marketing and R&D.

Just over 48 percent of the industry's exports were to the European Community in 1992. With $963 million in U.S. drug purchases, Japan represented the greatest single-country importer of U.S. pharmaceuticals. On the import side, the United States purchased $932 million in pharmaceuticals from the United Kingdom. Figure 3-8 shows U.S. pharmaceutical exports and imports for 1992.

The United States holds a dominant position in many international pharmaceutical markets. In Europe, for example, U.S. pharmaceutical companies account for 25 percent of total pharmaceutical sales. The United States also has a strong presence in Japan, with 10 percent of the market. Worldwide (including the United States), U.S. companies account for 33 percent of total pharmaceutical sales.[38] In important markets such as the United States, the United Kingdom, and France, U.S. companies have introduced the largest percentage of new drugs. Even in Japan, the United States is second only to Japan in new drug introductions.

As in many U.S. industries, foreign investment in U.S. pharmaceutical companies subsided in 1992 after peaking in the late 1980s. In 1990, foreign investment in U.S. pharmaceutical companies totaled $10 billion, while U.S. investment in foreign pharmaceutical companies totaled $10.6 billion.

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[38] FDA, 1990. *Op. cit.*

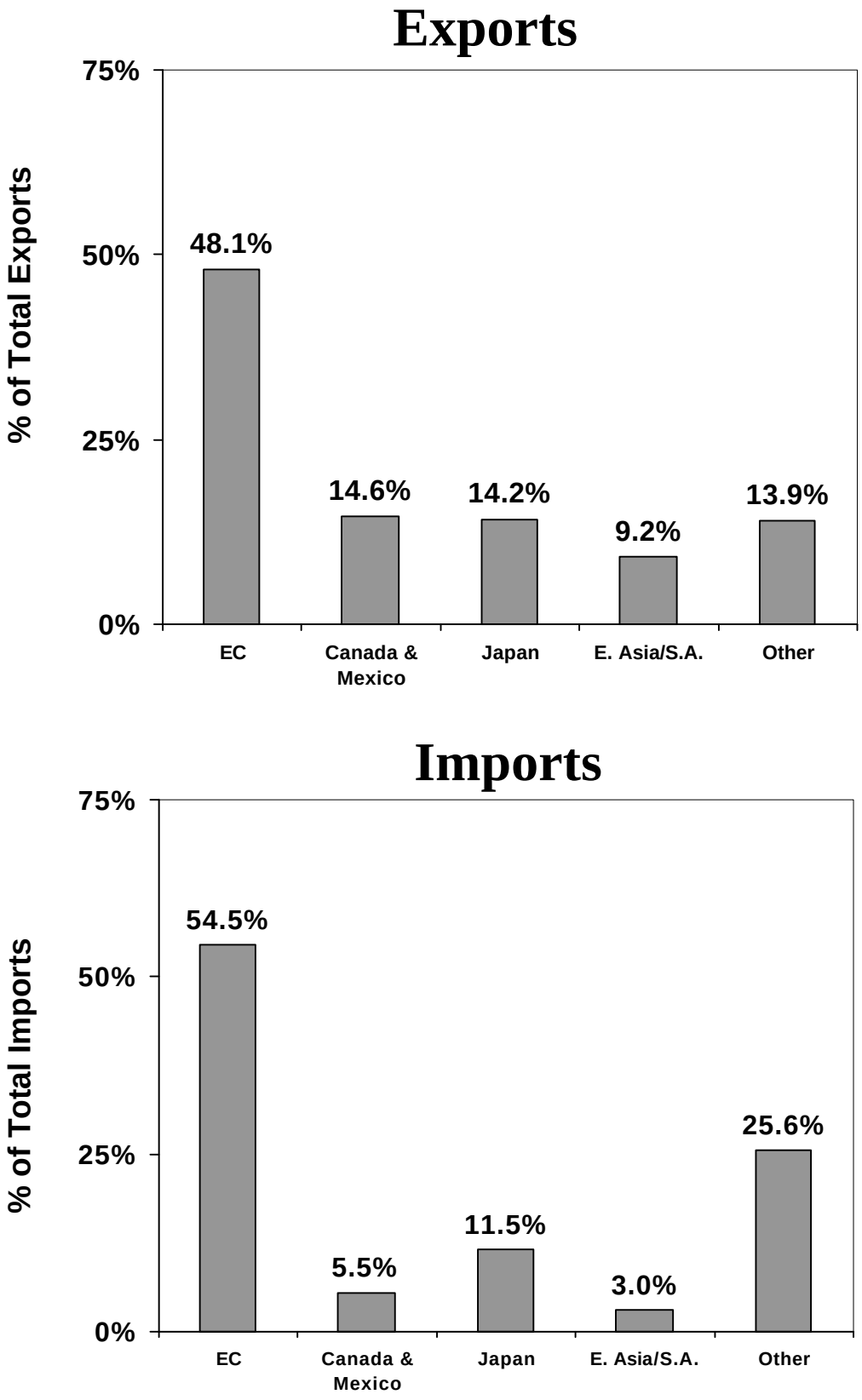

Figure 3-8. U.S. pharmaceutical exports and imports: 1992.

Source: U.S. Department of Commerce. 1994. *U.S. Industrial Outlook: 1994.* Washington, DC: U.S. Government Printing Office.

Despite the obstacles noted above, the U.S. Department of Commerce expects the United States to maintain a strong position in international markets over the next decade. Nearly 33 percent of worldwide pharmaceutical R&D is conducted by U.S. firms, thus providing the United States with a competitive edge for developing new drug products. The North American Free Trade Agreement (NAFTA), the advent of an economically unified Europe, and the increasing recognition of U.S. patent laws in China, Mexico, and Latin America, all suggest continued strength in international markets for the U.S. pharmaceutical industry. Greater political stability in the former Soviet Union and other Eastern Block countries also will create new trading opportunities for the U.S. pharmaceutical industry.

3.2.4.2 Survey Data

According to the Section 308 Survey data, international sales account for a significant proportion of the total revenues of surveyed facilities, owner companies, and parent companies. This finding is not surprising given the multinational character of the pharmaceutical industry (nearly 50 percent of the parent companies of surveyed facilities are headquartered in foreign countries). At the company level, international sales accounted for over 25 percent of all pharmaceutical revenues generated in 1990. Nearly 50 percent of all pharmaceutical sales made by parent companies in 1990 were to foreign countries. International sales are an important component of overall pharmaceutical sales at the facility level as well. Table 3-11 presents the distribution of surveyed facilities by percentage of pharmaceutical shipments accounted for by international sales. Although a substantial number (44 percent) of the surveyed facilities reported no international pharmaceutical sales, over 20 percent of the facilities reported receiving more than 10 percent of their pharmaceutical revenues from international sales in 1990. The mean pharmaceutical export rate for sample facilities was 8.8 percent in 1990.

3.2.5 Financial Conditions

The Section 308 Survey collected data on company costs, revenues, liabilities, earnings, and other financial statistics. These data allow key financial ratios to be calculated. The ratios are measures of a company's ability to meet short- and long-term obligations and to generate a sufficient return on investments. This section presents baseline data on two financial ratios: (1) rate of return on assets (ROA) and interest

Table 3-11

Number of Facilities by Percentage of Pharmaceutical Shipments Exported

Percentage of Pharmaceutical Shipments Exported	1989		1990	
	Number	%	Number	%
0%	82	46.9%	77	44.0%
>0%-2.5%	33	18.9%	36	20.6%
>2.5-5%	13	7.4%	13	7.4%
>5%-10%	11	6.3%	10	5.7%
>10%	36	20.6%	39	22.3%

Note: Only 175 facilities reported export data.

Source: Section 308 Pharmaceutical Survey.

coverage ratio (ICR), or times interest earned ratio. These ratios are similar to ratios used as part of the analysis in Section Six. They are presented here because these ratios can be easily compared to ratios developed for the pharmaceutical industry as a whole, and thus provide a comparison of the subgroup of firms affected by effluent guidelines to the larger pharmaceutical industry. In Section Six, similar ratios are used in an equation that allows the affected firms to be compared to the entire manufacturing sector, for both publicly and privately held firms.

The two financial ratios investigated in this profile are calculated at the owner company level only, where firm impacts are most direct and substantial. The ratios are also compared with industry benchmarks obtained from Dun & Bradstreet Information Services and Robert Morris Associates.

To attract the financing for a wastewater treatment system, a firm must demonstrate or project financial strength both before and after the regulation-induced investment. Financial strength is often assessed on the basis of whether a firm can incur debt associated with a capital investment while continuing to generate a return on investment that will attract further investment. Thus, measures of liquidity, debt levels, and profitability are critical to the analysis of financial strength.

The two ratios investigated here provide some evidence to potential creditors and investors on the affected firms relative to trends in the industry, although these ratios can be less helpful to analysts when one ratio looks “bad,” and the other ratio looks “good.” The analysis undertaken in Section Six solves this problem by combining a number of different ratios (which include return ratios and debt ratios) into an equation known as Altman’s Z, which gives varying weights to the different ratios on the basis of their ability to predict bankruptcy.

The sections below define the two ratios presented here (to provide a general comparison to the financial health of the affected firms relative to other firms in the industry) and discuss their value for this profile. Additionally, the discussion reviews the overall profitability of the industry, which helps to provide background for the remainder of the financial analysis.

3.2.5.1 Return on Assets

A firm's financial performance determines the willingness of creditors and investors to provide the capital necessary to sustain or expand operations. If performance is poor, investors will not provide capital or will seek higher returns in the form of higher interest rates on debt or higher returns on equity to compensate for above-average levels of risks. The higher cost of capital might in turn limit the ability of a given company to invest in improved wastewater treatment.

One aspect of financial performance can be measured in terms of the return on assets (ROA). ROA is computed as the ratio of net income to assets:

$$ROA = \frac{Net\ Income}{Total\ Assets}$$

ROA is a measure of profitability of a firm's capital assets, independent of the effects of taxes and financial structure. It is perhaps the most comprehensive measure of a firm's financial performance. ROA provides information about the quality of a firm's management, the competitive position of a firm within its industry, and, on an aggregate level, the economic condition of an industry overall. In addition, ROA incorporates information about a firm's operating margin and asset management capability: the ratio of net income to sales (operating margin), multiplied by the ratio of sales to assets (asset turnover), equals ROA. If a firm cannot sustain a competitive ROA, it will probably have difficulty financing new investments. This is true regardless of whether the financing is obtained through debt or equity financing.

Table 3-12 presents baseline ROA data for companies included in the survey sample. The ratio data are presented by quartile (i.e., with values given that denote the ratios for lowest 25 percent of firms, the median, and the highest 25 percent of firms) for firms grouped by annual revenues. The mean and standard deviation for each group of firms also are presented.

The return on assets over the years 1988 to 1990 varied from a first quartile of approximately -3 percent to an upper quartile of 10 percent for the smallest size class of firms (those with $25 million or less in annual revenues), to between 4 and 9 percent for the largest firms (those with over $1 billion in revenues). The data indicate that the lower quartile of firms in the smallest size class, on average, generated negative net income between 1988 and 1990. These firms appear to be the most vulnerable financially.

Table 3-12

Baseline Return on Assets (ROA) and Interest Coverage (ICR) Ratios, by Annual Revenues

Annual Revenues (Millions)	Number of Observations	Mean	Lower Quartile	Median	Upper Quartile
ROA					
0-25	60	-2%	-3%	5%	10%
26-200	55	5%	1%	5%	12%
201-1,000	33	15%	2%	7%	26%
>1,000	26	7%	4%	6%	9%
ICR					
0-25	60	Infinity	-1%	578%	51,267%
26-200	55	Infinity	201%	464%	8,470%
201-1,000	33	Infinity	272%	2,043%	Infinity
>1,000	26	1,111%	372%	677%	1,130%

Source: Section 308 Pharmaceutical Survey.

Long-term performance at this level would threaten these firms' ability to stay in operation. All other ROA values given in the table are positive.

Table 3-13 presents industry ROA ratios reported by Dun & Bradstreet for each SIC of the pharmaceutical industry. As can be seen, the results are more or less consistent with those drawn from the survey sample. Dun & Bradstreet's results reflect data for 266 companies overall. It should be noted that differences in the organization of data makes the comparison of ratio results only approximate. Comparing updated Dun & Bradstreet results with the 1990 data reveals an increase in ROA in all quartiles in the SIC 2833 pharmaceutical industry sector, suggesting that the financial condition of SIC 2833 pharmaceutical companies represented in the Dun & Bradstreet data strengthened in the early 1990s. The ROA data for other industry sectors are mixed, showing modest increases or decreases depending on the sector and quartile.

3.2.5.2 Interest Coverage Ratio

The second general area of concern to creditors and investors is the extent to which the firm can be expected to manage its financial burdens without risk of financial failure. In particular, if a firm's operating cash flow does not comfortably exceed its contractual payment obligations (e.g., interest and lease obligations), the firm is vulnerable to a decline in profits or an increase in costs because in either case its ability to continue meeting interest obligations would be in jeopardy. Either scenario may (1) sharply reduce or eliminate returns to equity owners of the firms, and/or (2) prevent the firm from meeting its contractual obligations.

The ability to manage financial commitments is expressed as the ratio of earnings before interest and taxes (EBIT) to interest obligations, or the interest coverage ratio (ICR):

$$ICR = \frac{EBIT}{Interest}$$

A low ICR indicates vulnerability of the firm to financial failure and the potential for difficulty in obtaining financing for wastewater treatment capital investments.

Table 3-13

Comparison of Sample Ratios with Published Industry Averages

Source	Number of Observations	Quartile		
		Lower	Median	Upper
ROA				
Survey Sample (1988-1990 average)	174*	-3% to 4%	5% to 7%	9% to 26%
Dun & Bradstreet Information Services (1990)				
SIC 2833	34	-2%	2%	11%
SIC 2834	167	3%	10%	21%
SIC 2835	29	NA	4%	7%
SIC 2836	34	0%	4%	10%
Dun & Bradstreet Information Services (1994)				
SIC 2833	44	4%	14%	22%
SIC 2834	202	3%	8%	17%
SIC 2835	36	-1%	1%	8%
SIC 2836	40	-4%	3%	11%
ICR				
Survey Sample (1988-1990 average)	174*	-1% to 372%	464% to 2,043%	1,130% to Infinity
Robert Morris Associates (1991-1992)				
SIC 2833	113	180%	440%	1,110%
Robert Morris Associates (1993-1994)				
SIC 2833	126	230%	710%	2,910%

*Out of 177 firms, only 174 responded with data for computing ROA and ICR.

Sources: Section 308 Pharmaceutical Survey data; Robert Morris Associates, 1994, 1992. *Annual Statement Studies*. Philadelphia, PA: Robert Morris Associates; Dun & Bradstreet Information Services, 1995, 1993. *Industry Norms and Key Business Ratios: Desk-Top Edition*. New York: Dun & Bradstreet.

As shown in Table 3-12, the interest coverage ratios vary from approximately -1 percent to 51,267 percent for the smallest firms to 372 percent to 1,130 percent for the largest firms in the Section 308 sample of firms. A number of firms reported no or negative interest burdens over the specified time period. These firms were assigned ICRs of infinity. Only the lowest quartile of companies in the smallest size class showed negative interest coverage ratios.

Robert Morris Associates reported data on the interest coverage ratios for 113 firms. As for ROA, these data are approximately consistent with those reported by the survey sample (see Table 3-13). The median value in the Robert Morris sample is 440 percent. Median values for the survey sample by size class ranged from 464 percent to 2,043 percent. Robert Morris Associates published updated ICR data in 1994.[39] Like Dun & Bradstreet's ROA figures for the pharmaceutical industry, these new ICR figures are higher than the 1991-1992 figures, again suggesting that the financial condition of pharmaceutical companies has strengthened.

3.2.5.3 Overview of Profitability in the Pharmaceutical Industry

This section presents additional evidence on profitability in the pharmaceutical industry. If the pharmaceutical industry were found to be relatively unprofitable overall, investment levels in the industry would be declining and industry benchmarks might underestimate the extent of vulnerability among industry firms. This is, however, not the case as can be seen in the discussion below and in the analysis of profit margins in Section Eight of this EA.

Profitability in the pharmaceutical industry has been extensively studied, and an OTA research report, *Pharmaceutical R&D: Costs, Risks and Rewards,* summarizes this work.[40] OTA compared the pharmaceutical industry's rate of return with that of other industries. OTA also considered whether the higher rates of return in the pharmaceutical industry were caused by a higher cost of capital in the industry. Elements of the OTA research are summarized here.

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[39] Robert Morris Associates, 1994. *Annual Statement Studies.* Philadelphia, PA: Robert Morris Associates.

[40] OTA, 1993. *Op. cit*

OTA compiled recent literature on the profitability and internal rates of return (IRR) for the pharmaceutical industry. The IRR is the interest rate at which the net present value of all cash flows into and out of the company equals zero. It provides a generally reliable method of calculating the return on investments. OTA identified a number of studies conducted between 1975 and 1991 that measured the profitability of the industry, including three studies that compared the pharmaceutical industry to others. These studies were designed to improve on the measurements possible with publicly available reports of industry profits. Accounting measures of profitability can be flawed because:

- Accounting standards require firms to record R&D, advertising, and promotion outlays as current expenditures, whereas they are generally investments with a future return. The value of the "intangible assets" represented by these expenditures is too uncertain for use in accounting statements but, nevertheless, represents assets that should be factored in.

- Financial statements report income and expenses as they are accrued and not necessarily as they are realized, which can distort the timing of revenues and investments and misrepresent the rate of return.

- Even if the other distortions are corrected, the accounting rate of return could still depart from the IRR because accounting profits do not adjust properly for the time profile of cash flows from various investments and are further distorted by growth or decline in investment over time.[40]

The studies identified by OTA used various techniques to develop more accurate estimates of the rate of return for the companies studied, such as incorporating information about the timing of investments in R&D, correcting for the effect of inflation, incorporating depreciation rates for investments in R&D and advertising, and other changes. The various studies produced estimates of the IRR.

Three studies compared the corrected pharmaceutical industry IRR estimates with similarly adjusted profit figures for other industries. The study results should be interpreted cautiously because they covered very small samples of companies. Further, the studies tended to focus on larger (and presumably more successful) firms; large pharmaceutical firms tend to be innovative, vertically integrated companies with high costs and relatively high profits, while smaller firms (e.g., many of those concentrating on the production of generics) tend to have competition and profit profiles that more closely resemble those of other

[40] OTA, 1993. *Op. cit.*

manufacturing industries. The studies found the adjusted rate of return for the pharmaceutical industry to be consistently higher than that in the other industries examined.

Table 3-14 summarizes the elements of the most recent of the studies reviewed by OTA, a study by Megan and Mueller of 10 pharmaceutical firms between 1975 and 1988. Megan and Mueller compared the IRR for the pharmaceutical industry with that of other industries that have similarly large investments in R&D and advertising, including the toy, distilled beverages, and cosmetics industries. These authors used various assumptions about the depreciation of R&D and advertising to measure the true profitability impact of these investments. This study found that 10 pharmaceutical firms had an IRR of 12.15 percent. The other industries, with similarly adjusted depreciation estimates, produced rates of return of 6.6 percent (toys), 11.44 percent (distilled beverages), and 11.5 percent (cosmetics).

OTA also commissioned its own report on the relative level of pharmaceutical industry profits. This study, authored by Baber and Sok-Hyon, used a recently developed technique for converting accounting data into an IRR estimate. This study compared rates of return for 54 research-intensive pharmaceutical firms with samples of companies in other industries. The authors found that the pharmaceutical industry had IRRs that were consistently 2 to 3 percentage points higher, under various alternative calculation methodologies, than those for nonpharmaceutical companies.

The question remains whether the observed differences in IRR resulted from differences in the cost of capital. If pharmaceutical investments are riskier, investors would require higher IRR and the cost of capital for the industry would be higher. OTA estimated the average cost of capital for the industry and for two control groups. OTA found that the pharmaceutical industry's cost of capital was slightly higher than that for one group of control firms and lower than that for another group. OTA recognized the potential errors and biases in its measurement techniques, but nevertheless concluded that the higher rates of return found for the pharmaceutical industry could not be explained by differences in the relative costs of capital.

Overall, the profitability of the pharmaceutical industry appears to be above average among U.S. industries. This suggests that the overall baseline viability of the industry is equivalent to, if not better than, that of other industries. This finding is also supported in Section Eight of the EA, in which the median profit

Table 3-14

Summary of Megan and Mueller Pharmaceutical Industry Profits Study

Study Description	Study Characteristics	Comment
Pharmaceutical industry sample (year of data)	10 major firms (1975 to 1988).	
Other industries sample	Selected firms in advertising or R&D-intensive industries; 6 firms in toy industry; 4 in distilled beverage firms; 9 in cosmetic firms.	Selected firms with similar large investments in R&D and advertising.
R&D capitalization assumptions	R&D depreciation rates estimated for each firm by regressing sales on lagged R&D. Maximum 8-year life for investment.	Capitalization rate assumptions are necessary to improve accuracy of rate of return estimates over normal accounting measures.
Advertising capitalization assumptions	Same depreciation estimation technique as for R&D with a maximum 4-year life for investment.	Capitalization rate assumptions are necessary to improve the accuracy of rate of return estimates over normal accounting measures.
Rate-of-return estimates—pharmaceutical industry	12.15%	
Rate-of-return estimates—other firms	Toy industry - 6.66% Distilled beverages - 11.44% Cosmetics - 11.51%	Other industries showed lower rates of return, using consistent adjustments to the accounting data.

Source: U.S. Congress, OTA. 1993. *Pharmaceutical R&D: Costs, Risks, and Rewards*. Washington, DC: U.S. Government Printing Office.

margin of the affected firms (posttax EBIT/revenues) is shown to be substantially higher than U.S. industry averages (7.4 percent vs. 4.9 percent).[41]

3.3 INDUSTRY STRUCTURE AND THE PHARMACEUTICAL MARKET

Information concerning market structure, the demand for pharmaceuticals, and pricing behavior provides much of the basis for reaching conclusions about the industry's ability to "pass through" additional regulatory costs via higher drug prices and thereby predicting which entities bear what portions of regulatory impacts. The first section of the following discussion (Section 3.3.1) examines the pharmaceutical industry's market structure as defined by barriers to entry, industry concentration ratios, and vertical integration patterns. Subsequent sections examine the characteristics of pharmaceutical demand (Section 3.3.2) and market conduct and performance (Section 3.3.3). Section 3.3.4 presents conclusions about the likelihood that manufacturers can pass through regulatory costs to consumers of pharmaceuticals.

3.3.1 Market Structure

The more barriers to entry that exist in a given market, the more likely it is that monopolistic or oligopolistic conditions will prevail in that market. Such conditions allow firms greater latitude in setting prices and hence the ability to pass regulatory costs along to consumers. Barriers to entry and concomitant factors of concentration and vertical integration are discussed in the following sections.

3.3.1.1 Barriers to Entry

Critics of the pharmaceutical industry often blame barriers to entry (i.e., economic, social, and regulatory factors that prevent or discourage new firms from entering a given market) for limiting competition in the pharmaceutical industry and thereby creating inefficiencies in the supply of a socially desirable product.

[41] Section 308 Pharmaceutical Survey and Johnston, Daniel, 1992. *Oil Company: Financial Analysis in Nontechnical Language*. Tulsa, Oklahoma: PennWell Books.

High Cost of Pharmaceutical R&D

Major barriers to entry are the high cost of pharmaceutical R&D, the cost of preparing FDA applications,[42] and the length (and thus cost) of the R&D and regulatory review process, especially for innovative companies wishing to enter the new drug market; the cost (and process length) of R&D for generic and OTC drug licensing and manufacturing are lower, although still significant. Many established firms with drugs already on the market rely heavily on profits from sales of their existing drugs (as well as outside investors) to fund more R&D to create a "pipeline" of products that, when approved, will then fund more R&D. Without a pre-existing profit stream and capital resources, new firms must attract investors who can tolerate long-term, high-risk investments. Some investors are more inclined to invest in established firms that have demonstrated that they can bring a drug to market, recover R&D expenditures, and produce reasonable returns on investment capital. Some investors also might be wary of new firms that have not demonstrated that they can clear FDA regulatory hurdles, although many new firms overcome this issue by hiring regulatory affairs professionals from established firms or by contracting with outside companies specializing in handling pharmaceutical regulatory matters.

Nevertheless, many investors, anticipating large profits if a new drug is successful, are willing to invest substantial sums in new pharmaceutical firms over a period of a decade or more. Indeed, this factor accounts for the rapid proliferation of biotechnology firms over the past two decades, when advances in genetics and recombinant DNA technologies have made possible the development of recombinant DNA drugs and other gene/immunological products of potential value in treating a wide range of diseases, such as cancer, acquired immune deficiency syndrome (AIDS), Lou Gehrig's disease, asthma, diabetes, heart disease, multiple sclerosis, rheumatoid arthritis, Lyme disease, stroke, and viral infections, among others. Many biotechnology firms started in the 1970s and 1980s by scientists from established companies, academia, or research institutes have been fully funded by investors for more than a decade. Only now are some of these firms beginning to produce marketable products, yet most firms are still largely supported by investors. Analysts, however, expect a significant number of biotechnology products to come to market over the next several years and beyond, during which time investors hope to more than recoup their investments.

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[42] As noted earlier, drug sponsors must now pay FDA to review their applications, further increasing the cost of the R&D and the regulatory review process.

Recently, publication of disappointing results for a few biotechnology drugs in early clinical trials has dampened venture capitalists' enthusiasm for biotechnology companies. As a result, some companies have developed strategic partnerships or other deals with established innovative pharmaceutical companies that have money, manufacturing capacity, and sales/distribution avenues but a shortage of innovative products. Such partnerships are viewed as benefiting both parties—providing a reliable source of capital for one, and a new source of potentially highly profitable products for the other. In the new climate of cost and time pressure, biotechnology companies are expected to move more quickly and efficiently in the 1990s and beyond, but are still expected to flourish with the help of some combination of venture capital investment and pharmaceutical corporate partnerships.

Patents

By law, patented drugs in the United States enjoy ostensible protection from bioequivalent drugs for a period of 17 years.[43] This protection gives the drug manufacturer a monopoly over its particular product for the life of the patent. Several factors, however, act to reduce the effective patent life of drugs. The greatest threat to the effective patent protection for a drug is the delay between patent issuance and FDA approval, which can be as much as 10 years. Drug companies obtain patents during the R&D phase, and many years can elapse before the company can take advantage of its monopoly power. OTA estimates that the effective patent life (i.e., the time between drug approval and patent expiration) on new drugs averages 11 years.[44]

Although patents give manufacturers a monopoly over new drugs for the life of the patent, preventing new (or established) firms from entering the market for those specific drugs, patents do not provide protection from competition because competitors may and often do offer other drugs with similar therapeutic benefits. As illustrated in the example in Section 3.1.2, a new drug can face stiff competition from other branded, patented drugs and generic drugs in the same therapeutic class. In some of the largest therapeutic classes (e.g., anti-infectives and antihypertensives), competition is intense.

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[43] OTA, 1993. *Op. cit.*

[44] *Ibid.*

Once patents expire, manufacturers of bioequivalent, or generic, drugs can enter the market. Evidence suggests that over the past decade, introduction of generic versions of branded products is becoming more common. Today, nearly 34 percent of all prescription drug orders are filled by generics rather than branded, or "pioneer" drugs, an 11 percent increase since 1986. As noted earlier, the passage of the 1984 Price Act made it easier for generics to gain market approval from FDA, and both public and private insurers have become more adamant about the use of less expensive generics.

High Promotional Expenditures

High promotional expenditures in the pharmaceutical industry also can serve as a barrier to entry. Traditionally, the economic literature has viewed high promotional expenses as an indication of an imperfect competitive environment. In a market characterized by oligopoly (i.e., the domination of a given market by a small number of firms), firms will use advertising rather than price competition to differentiate products.

As noted earlier, however, proponents of pharmaceutical advertising argue that such advertising plays a crucial role in a market in which both clinical and cost issues are central to prescribing and purchasing decisions. In this setting, advertising serves to educate physicians and consumers about clinical features that make individual drugs more or less suitable—and more or less cost-effective—for specific patients. For example, the marketer of a branded, patented drug might provide published studies demonstrating that the drug is associated with a lower rate of side effects, complications, recurrences, or relapses than a generic drug (or a less expensive branded drug) in the same therapeutic class. Taking into account the cost of treating these undesirable outcomes, the total cost of treatment with the drug is actually less than the total cost of treatment with the generic—although more expensive on a unit price (or cost per course of therapy) basis; thus, the branded drug is more cost-effective than the generic. Increasingly, pharmaceutical firms are using promotional expenditures to demonstrate (and compete on the basis of) cost-effectiveness rather than unit drug price.

Regardless of how high promotional expenditures in the pharmaceutical industry are explained, one might expect new firms to be at a disadvantage with respect to more established firms if they must invest significantly in advertising to compete. The high promotional expenses required to compete add to the capital demands on new entrants. Despite the high cost of promotion, several economists in the late 1970s

determined empirically that industry promotional expenditures were positively related to market entry. Thus, new entrants use their promotional campaigns to achieve market entry. In a study of 17 therapeutic markets over the period 1969 to 1972, Tessler concluded that promotional expenditures actually facilitate entry because new products could not compete with existing products without being able to distinguish themselves through advertising.[45] Hornbrook found similar results and concluded that promotional expenditures serve more as a market penetration tool for new pharmaceutical manufacturers than as a barrier to entry.[46]

The three barriers to market entry discussed here—the high cost and substantial time involved in R&D, patent protection, and high promotional expenditures—clearly are not insurmountable, nor are they exclusively hindrances. Although it is extremely difficult to quantify the impact of such barriers on market competition, it is likely that established pharmaceutical companies have a degree of market power because of their established R&D operations and regulatory experience, patent protection, and reputations. Although the number of pharmaceutical establishments, particularly generics manufacturers, has grown over the past several decades, it is likely that competition in the industry would have been greater in the absence of the barriers to entry discussed above.

3.3.1.2 Concentration and Vertical Integration

The degree of concentration and vertical integration in a given industry is often used as an indicator of barriers to entry. Concentration is generally measured in terms of the percentage of value of shipments accounted for by a given number of firms in a particular industry. The U.S. Department of Commerce calculated 4-, 8-, 20-, and 50-firm concentration ratios for all 4-digit SIC industries through 1992 (see Table 3-15). The higher the concentration ratio in a given industry, the easier it is for manufacturers to set prices or to collude to set prices. Industrial economists have proposed that when the leading four firms control 40 percent or more of a given market, the market may be characterized by oligopolistic conditions that present significant barriers to entry.

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[45] As cited in Feldstein, Paul J., 1988. *Health Care Economics*. 3rd Edition. New York, NY: John Wiley & Sons.

[46] *Ibid*.

Table 3-15

4-, 8-, 20-, and 50-Firm Concentration Ratios:
SICs 2833, 2834, and 2836: 1954-1992

SIC Code	Year	Percent of Total Value of Shipments			
		4 Largest Companies	8 Largest Companies	20 Largest Companies	50 Largest Companies
2833 Medicinals and Botanicals	1992	76	84	91	97
	1987	72	80	89	95
	1982	62	75	85	94
	1977	65	78	89	96
	1972	59	75	90	98
	1970	64	74	NA	NA
	1967	74	81	91	98
	1966	70	81	NA	NA
	1963	68	79	91	99
	1958	64	77	89	98
	1954	72	84	93	NA
2834 Pharmaceutical Preparations	1992	26	42	72	90
	1987	22	36	65	88
	1982	26	42	69	90
	1977	24	43	73	91
	1972	26	44	75	91
	1970	26	43	NA	NA
	1967	24	40	73	90
	1966	24	41	NA	NA
	1963	22	38	72	89
	1958	27	45	73	87
	1954	25	44	68	NA
2836 Biological Products, Except Diagnostics	1992	53	71	86	96
	1987	45	65	80	93

NA = Not Available.
Source: U.S. Department of Commerce, 1995. *U.S. Census of Manufactures: 1992.* MC92-S-2. Washington, DC: U.S. Government Printing Office; U.S. Department of Commerce, 1991. *U.S. Census of Manufactures: 1987.* MC87-S-6 (CD-ROM). Washington, DC: U.S. Government Printing Office.

Table 3-15 lists the 4-, 8-, 20-, and 50-firm concentration ratios for SICs 2833, medicinal and botanicals; 2834, pharmaceutical preparations; and 2836, biological products, as reported by the U.S. Department of Commerce. As can be seen, the four leading firms in SIC 2833 controlled 76 percent of sales of SIC 2833 products in 1992. This situation contrasts to the four-firm concentration ratio of 26 percent in SIC 2834 and 53 percent in SIC 2836. There are almost three times as many companies in SIC 2834 as in SIC 2833. The relatively low four-firm concentration ratio of 26 percent in SIC 2834 and the relatively large number of companies suggests that barriers to entry in the pharmaceutical preparations sector of the industry are relatively insignificant compared with barriers to entry in the medicinals and botanicals sector. All of the concentration ratios increased between 1987 and 1992. These data suggest that the mergers, increased formation of megacompanies, strategic alliances/mergers with insurance companies, and selloffs of divisions of small- to medium-size companies in the late 1980s and early 1990s have increased vertical integration and concentration in the pharmaceutical industry.

Nevertheless, concentration ratios calculated for such large industry segments are of limited value. The overall drug market is fragmented into a number of separate, noncompeting therapeutic markets. Manufacturers of antibiotics, for example, do not compete with manufacturers of muscle relaxants. Thus, concentration ratios should be calculated and analyzed within the specific therapeutic markets in which manufacturers do compete. Only one study was identified in the economic literature of concentration ratios by therapeutic category. The study, conducted by Vernon, divided the prescription drug market into 19 therapeutic markets according to the degree of demand-side substitutability between different drugs (i.e., relatively close drug substitutes were placed in the same general therapeutic market).[47] The four-firm concentration ratios calculated by Vernon in the 19 therapeutic markets are presented in Table 3-16. As can be seen, all of the concentration ratios are quite high; the lowest ratio in a therapeutic market is 46 percent. Several concentration ratios are in the 90 percent range, and the unweighted average is 68 percent. Vernon's study suggests that a relatively small number of companies dominate sales in the individual therapeutic markets.

Even therapeutic market-specific concentration ratios might not present an accurate picture of competitive conditions in the pharmaceutical industry, however. According to Feldstein, concentration ratios

[47] Vernon, John M., 1971. Concentration, Promotion, and Market Share Stability in the Pharmaceutical Industry. *Journal of Industrial Economics* 19:246-266. July 1971.

Table 3-16

Concentration Ratios in the U.S. Prescription Drug Industry, By Therapeutic Market: 1968

Therapeutic Market	Four-Firm Concentration Ratio
Anesthetics	69
Antiarthritics	95
Antibiotics-penicillin	55
Antispasmodics	59
Ataractics	79
Bronchial dilators	61
Cardiovascular hypertensives	79
Coronary-peripheral vasodilators	70
Diabetic therapy	93
Diuretics	64
Enzymes-digestants	46
Hematinic preparations	52
Sex hormones	67
Corticoids	55
Muscle relaxants	59
Psychostimulants	78
Sulfonamides	79
Thyroid therapy	69
Unweighted average	68

Source: Vernon, John M., 1971. Concentration, Promotion, and Market Share Stability in the Pharmaceutical Industry. *Journal of Industrial Economics* 19:246-266. July, 1971.

are a static measure of market power.[48] Feldstein notes that although a particular therapeutic market can be characterized by high concentration at a given point in time, market shares in that therapeutic market can change radically over time. Instability in market shares over time indicates intense competition among firms through new product innovation. One study in the early 1970s noted that of the 20 industries investigated, only the petroleum industry possessed a higher degree of market instability than the pharmaceutical industry. Moreover, exit from and entry to the pharmaceutical industry seems to be quite high. In a study of 17 therapeutic markets between 1963 and 1972, 15 markets had five or more new entrants. Market exit occurred in 16 of the 17 markets.[49]

A high level of vertical integration might also indicate the presence of barriers to entry in a given industry. Vertical integration refers to the extent to which production inputs and services are produced and transferred within a given company, rather than procured from other companies. In the pharmaceutical industry, a vertically integrated firm might engage in R&D, several types of manufacturing (e.g., bulk drug manufacturing and finished product formulation), and marketing/ distribution. In the pharmaceutical industry, the two principal advantages of vertical integration are in ensuring confidentiality and achieving economies of scale.

Although production contracts with other companies contain confidentiality provisions, some firms choose vertical integration as a way of ensuring confidentiality, especially important when developing and launching new innovative drugs. Economies of scale occur when production inputs can be used to produce several different outputs. For example, cumulative drug R&D and promotional expenditures might be used jointly in the production of more than one drug product. Similarly, R&D studies, manufacturing processes, and regulatory experience established during the development and marketing of a branded drug might later be used to bring a generic equivalent to market very quickly and efficiently upon expiration of the branded drug's patent protection. Such economies of scale might serve as a barrier to entry in the pharmaceutical industry to the extent that the high costs associated with pharmaceutical R&D and promotion raise start-up

[48] Feldstein, 1988. *Op. cit.*

[49] *Ibid.*

costs and reduce the ability of new firms to raise sufficient capital to profitably enter the industry.[50]

Evidence from the Section 308 Survey provides some indication that pharmaceutical companies are vertically integrated. Of the 139 parent companies for which survey data are available, 129 have operations spanning all four of the industry's major production processes: fermentation (process A), biological and natural extraction (process B), chemical synthesis (process C), and formulation (process D). Three of the parent companies own facilities involved in processes A or C only, and 7 own facilities involved in processes B or D only. At the facility level, 150 of the 244 facilities surveyed engage in only one production process (101 of these firms engage only in formulation), 70 perform two production processes, 16 perform three production processes, and 8 engage in all four major production processes. Nearly 85 percent of the owner and parent companies reported R&D expenditures in the 3 years surveyed.

These data suggest that many pharmaceutical companies have chosen to integrate vertically, engaging in R&D, production of active ingredients, and formulation to take advantage of natural economies of scale that reduce the costs associated with developing and marketing new drugs. The surveyed pharmaceutical companies are not necessarily representative of the industry as a whole, however, because the survey focused on wastewater dischargers. As noted earlier, this group includes a greater proportion of large establishments—and probably a greater proportion of vertically integrated firms—than does the industry as a whole. Nevertheless, some degree of vertical integration clearly exists, and the survey data agree with observations that many major pharmaceutical companies are vertically integrated. As noted above, recent mergers of major pharmaceutical firms appear to have increased the size and degree of vertical integration of large firms, while recent sales of R&D or other divisions by smaller firms may have decreased the size and degree of vertical integration of those firms.

The effect of vertical integration on market structure and market performance cannot be quantified, but the data suggest that major pharmaceutical companies have a degree of market power. In fact, some analysts are predicting that one aspect of the trend toward greater vertical integration—the establishment of generic manufacturing divisions within major innovative pharmaceutical companies—may jeopardize the

[50] Vertical integration also can lead to economies of scale where the existence of fixed factors of production such as physical capital can cause unit costs to fall as output rises. It is generally assumed, however, that unit costs are constant across output levels in the pharmaceutical industry. Other advantages of vertical integration might include the ability to capture monopoly/monopsony inefficiency losses and engage in price discrimination (RTI, 1993. *Op. cit*.)

future of small independent generics firms, which might not be able to compete against large firms with much greater resources (see Section 3.3.3.1). If this trend continues as projected, the number of small generics firms might decline significantly.[51] A more recent report in the *Wall Street Journal* suggests that intense competition among the small independent firms and larger firms has, in fact, hurt some of the small firms; by contrast, the report indicates that small generics firms selling products with relatively little competition (including products in niche markets) are prospering.[52]

3.3.2 The Characteristics of Demand for Pharmaceuticals

Demand conditions for pharmaceutical manufacturers will help determine the impact of regulation-induced costs on market prices and outputs. This section examines various characteristics of demand, including the market demographics, the primary market outlets, and the effect of health insurance on the market.

Demand conditions vary significantly among specific drug markets. Differences in regulatory requirements and payment mechanisms are particularly important in determining demand. For example, in the prescription drug market (i.e., new drugs and generics), demand is complicated by the role of health care providers and the presence of health insurance. Unlike most consumer markets, consumers of prescription drugs are not directly involved in purchasing decisions; that is, they do not decide which drugs to take, for how long, and at what dosages. Health care providers act on the patient's behalf in deciding which medical treatment is most appropriate given the patient's health status, financial condition, and insurance coverage. These topics are discussed further below.

The demand for OTC (i.e., nonprescription) drugs, on the other hand, conforms more readily to standard models of consumer demand. OTC drugs are relatively easy to market, available without physician consent, and sold in a relatively competitive environment. Like the demand for other nondurables, the demand

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[51] Ukens, Carol, 1994. The Generic Industry '94: It's a Jungle Out There. *Drug Topics Supplement 1994*; Giltenan, Ed, 1994. The Copycat Shuffle. *Pharmaceuticals '94.* March 7.

[52] Eisinger, Jesse, 1996. Makers of Generic Drugs Are Expected to Post Mixed Results for First Quarter. *The Wall Street Journal.*

for OTC drugs is thought to be positively correlated with income and negatively correlated with price. Consumers identify a specific health need, such as relief from minor pain or cold symptoms, and then search for a product to satisfy that need. Because in most cases a variety of OTC products will meet a given need, demand is heavily influenced by advertising and price.

3.3.2.1 Market Demographics

Like the demand for health care generally, the demand for pharmaceuticals is derived from the demand for good health. A pharmaceutical is both a consumption commodity, since it makes the consumer feel better in the present, and an investment commodity, since it may extend the life of the consumer. Given this view of pharmaceutical demand, one would expect, all other things being equal, that the demand for pharmaceuticals will be dependent on factors such as the incidence of illness and sociodemographic factors like age, education, and income. Other factors, such as perceptions of the seriousness of medical conditions and belief in the efficacy of medical treatment, also influence pharmaceutical demand.

Among individuals, pharmaceutical demand is heavily concentrated in the segment of the population that includes people of age 65 and older. In fact, today between 30 and 40 percent of all pharmaceuticals are consumed by persons 65 years old and older.[53] This finding is not surprising given the strong correlation between age and health. As the U.S. population ages over the next several decades, the demand for pharmaceuticals will presumably rise. Since 1980, the number of people age 65 and older has increased at a rate more than twice that of the general population. By 1996, the U.S. Census Bureau predicts that 13 percent of the U.S. population will be over 65 years of age. The U.S. Department of Commerce cites the aging of the U.S. population (and the resulting growing market for chronic care medicines) as one of the main reasons it expects pharmaceutical sales to grow over the next few years.[54]

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[53] NatWest, 1992. *Op. cit.*

[54] U.S. Department of Commerce, 1993. *Op. cit.*; U.S. Department of Commerce, 1995. *Op. cit.*

3.3.2.2 Major Market Outlets

According to a 1991 study of the pharmaceutical market, retail and hospital pharmacies dispense over 84 percent of all pharmaceuticals sold in the United States (see Figure 3-9). Direct mail order establishments and HMOs, however, are capturing an increasing share of the market. Pharmaceutical purchases by hospitals have fallen by 6 percent since 1983. This drop is credited, in part, to changes in the Medicare system that have created incentives for hospitals to reduce inpatient services. Drugs once prescribed on an inpatient basis are now more likely to be prescribed on an outpatient basis and thus dispensed through retail pharmacies.[55]

3.3.2.3 The Role of Health Insurance and Health Care Providers

The demand for prescription drugs is influenced by the complex structure of health insurance and health care provision. It is generally believed that the presence of health insurance makes consumers relatively insensitive to the price of health care. Although not empirically measured, this relationship is expected to apply to the demand for pharmaceuticals as well. The full impact of health insurance on prescription demand is somewhat muted by deductibles and copayments; nonetheless, health insurance almost certainly makes consumers less sensitive to drug prices. As was noted many times during the recent health care reform debate, many privately insured Americans are protected from extraordinary medical costs and, thus, have little incentive to limit health care expenditures, including the use of prescription drugs. According to OTA, in 1987, 28 percent of all prescribed drug expenditures were paid for by private insurance, 10 percent by Medicaid, 6 percent by other insurers such as Medicare and Worker's Compensation, and 57 percent by individuals.[56]

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[55] OTA, 1993. *Op. cit.*

[56] Insurance coverage of pharmaceutical expenditures is less than that for health care generally. Approximately 75 percent of all health care expenditures are paid for by insurance; *ibid.*

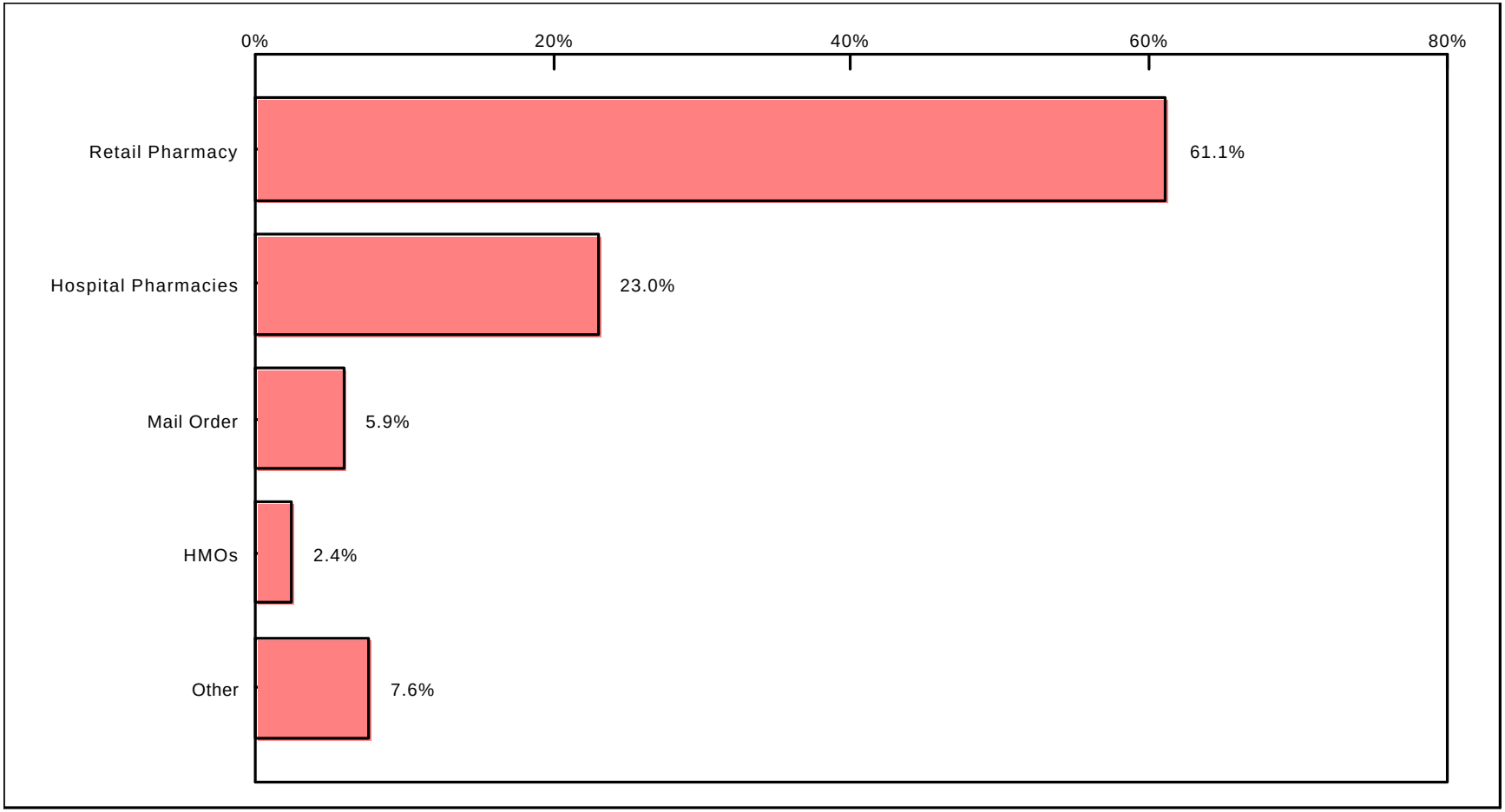

Figure 3-9. U.S. Pharmaceutical sales by retail component: 1991.

Source: U.S. Congress, Office of Technology Assesment, 1993. *Pharmaceutical R&D: Costs, Risks, and Rewards.* Washington, DC: U.S. Government Printing Office.

The percentage of Americans with public or private health insurance has risen steadily over the past decade to 86 percent today.[57] Virtually all health insurance plans cover hospital services, including prescription drugs administered at the hospital. As noted earlier, however, hospitals account for a declining share of total pharmaceutical sales in the United States, dropping from 29 percent in 1983 to 23 percent in 1991.[58] This drop can be attributed to a shift toward a greater reliance on outpatient services, which are often less expensive than hospital care.

Outpatient prescription drug insurance, although less common than inpatient coverage, covers an increasing proportion of Americans. The proportion of outpatient prescription drug purchases paid for by insurers increased from 27 to 43 percent between 1977 and 1987.[59] OTA estimates that in 1987, between 70 and 74 percent of the noninstitutionalized population had at least some outpatient prescription drug coverage. Very few health insurance plans cover 100 percent of prescription drug costs, however. Full coverage is most common in HMOs. Most health insurance plans rely on copayments to limit prescription drug use, although copayments are generally in the range of $5 or less.[60] Private insurers generally cover all drugs approved for market by FDA.[61]

The lack of price sensitivity among consumers is partly offset by increasing sensitivity among insurers. To control rising health care costs, many private and public insurers have moved to limit pharmaceutical expenditures. Many private insurers have created incentives for physicians and consumers to substitute generic drugs for branded drugs. OTA reports that in 1989, 14 percent of all employer-based health insurance plans offered lower copayments for generic drugs than for branded drugs. HMOs are particularly well suited to encourage generic drug utilization because they control physicians more directly than fee-for-service plans. Some HMOs require that their pharmacies automatically substitute generic drugs

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[57] OTA, 1993. *Op. cit.*

[58] *Ibid.*

[59] *Ibid.*

[60] *Ibid.*

[61] Insurance does not always cover uses of prescription drugs not explicitly approved by FDA. OTA reports that insurers are generally willing to reimburse for "off-label" uses that have been documented as effective in one of three major medical compendia or in multiple published studies. The so called off-label use of prescription drugs is common in many branches of medicine, especially in the treatment of cancer; *ibid.*

for branded drugs unless the physician explicitly instructs otherwise. HMOs and other insurers also try to reduce drug costs by negotiating with manufacturers for volume discounts and relying on direct mail-order pharmacies for drugs that patients need refilled on a regular basis. In fact, the U.S. Department of Commerce cites reports from economic research firms suggesting that the formation of large buying groups under managed care programs has served to moderate prescription drug prices; a more recent report from an industry analyst agrees with this finding.[62] Medicaid, the nation's major public health insurer, also creates incentives to keep drug costs low.

3.3.2.4 Substitutability Among Pharmaceuticals and With Other Medical Services

The availability of close substitutes plays an important role in determining competitive conditions in various drug markets. Generally, the greater the availability of close substitutes in a given market, the more difficult it is to raise prices without losing market share. Substitution occurs within specific drug markets or within the overall health care market (i.e., pharmaceuticals can substitute for other forms of health care), and both of these are discussed below.

Substitutability Among Pharmaceuticals

The degree of substitutability within or across specific drug markets varies considerably between the patented drug market, the generic drug market, and the OTC drug market.

Patented Drug Market. Patented drugs in the United States enjoy ostensible protection from bioequivalent drugs for a number of years. Effective patent life, however, reflects only the period of time in which a particular compound is formally protected from bioequivalent competitors. Manufacturers of patented drugs may enjoy market exclusivity for many years after patent expiration because of the time needed to approve generic competition, or because the particular market is too small to entice generic

[62] U.S. Department of Commerce, 1994. *Op. cit.*; Moore, 1996. *Op. cit.*

competitors.[63] In addition, manufacturers of patented drugs may be able to extend their monopoly power after patent expiration by developing new dosage forms for the same drug. The 1984 Price Act automatically grants a 3-year period of market exclusivity, regardless of patent status, to any drug for which an additional full NDA or NDA supplement has been submitted. With a new dosage form that makes a drug easier to administer or causes fewer side effects, the "pioneer" manufacturer can retain effective monopoly power because its competitors can only market the earlier, and presumably inferior, generation of the product.

The availability of close substitutes for many patented drugs, however, significantly erodes the monopoly power enjoyed by these manufacturers. Drugs of different molecular structure often can compete in the same therapeutic market. For example, four classes of drugs (calcium channel blockers, angiotensin-converting enzyme inhibitors, beta-blockers, and diuretics, each of which contains several branded drugs) all compete in the mild-to-moderate antihypertension drug market; additional classes of drugs compete in the moderate-to-severe antihypertension drug market. Between 1987 and 1992, 78 percent of the new drugs approved by FDA were deemed substantially equivalent to already marketed drugs in terms of medical importance and therapeutic usage.[64] Thus, it would seem that although patents certainly reduce the availability of identical substitutes during the life of the patent, physicians in many cases can choose from more than one drug therapy to treat a given ailment.

Generic Drug Market. The ascendancy of generic competitors in the prescription drug market has greatly increased the availability of substitutes in the nonpatent drug market. Prior to the 1984 Price Act, generics accounted for a low percentage of total prescriptions given their relatively low price and FDA-guaranteed bioequivalence. Brand loyalty, strict FDA regulation, and state antisubstitution laws that prevented pharmacies from making generic substitutions not specifically requested by a physician all acted to reduce the ability of generics to compete with branded prescriptions. Over the past decade, however, generic competition has increased dramatically, and today generics account for 34 percent or more of all prescriptions written.

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[63] U.S. patent law prohibits companies from conducting commercially valuable research using patented products.

[64] FDA, 1992. *Op. cit.*

The rise in generic competition is the result of several factors. Perhaps most importantly, both private and public insurers (i.e., Medicaid/Medicare) encourage, if not require, physicians to prescribe generic drugs when available (virtually all states have repealed their antisubstitution laws). Many HMO pharmacies now automatically prescribe generic drugs unless the physician makes a handwritten request for a branded drug. As mentioned earlier, the 1984 Price Act made it easier for generics to obtain FDA approval as well. In a recent study of 18 drugs whose patents expired in 1983, Grabowski found that nearly all of the manufacturers lost about half of their market share to generic competition within 2 years after initial entry of generic competitors.[65]

OTC Market. As discussed earlier, the OTC market is much like other competitive commodity markets where there is a high degree of substitutability and demand is relatively sensitive to changes in price. OTC drugs do not face the same regulatory hurdles as prescription drugs and generally do not require such large R&D expenditures. Unlike many prescription drug markets, most OTC drug markets are quite large and thus capable of sustaining many manufacturers of the same product.

Substitutability With Other Medical Services

Physicians typically can serve the patient in the hospital setting or they can provide ambulatory (i.e., outpatient) services, such as prescription medicines. For certain conditions, pharmaceuticals might be a very close substitute for inpatient services (e.g., hospitalization, surgery). For example, instead of performing surgery, a doctor might prescribe antibiotics to treat infected tonsils or antibiotics plus renally acting drugs to treat a benign enlargement of the prostate gland. Alternatively, a doctor might prescribe medications as a means of reducing hospital stays for surgery; for example, use of antibiotics to prevent infection can reduce the length of stay required for many types of surgery, while use of blood cell growth factors can reduce the length of stay required for bone marrow transplants (which are among the most expensive procedures performed in hospitals today). In addition, the use of medicines reduces the prevalence of some medical conditions that might otherwise require expensive hospital treatment; for example, the use of vaccines

[65] Grabowski, Henry G., and John M. Vernon, 1992. Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Drug Act. *Journal of Law and Economics* 35(2):331-350. October 1992.

reduces the prevalence of infectious diseases such as polio, diphtheria, and hepatitis, while the use of antihypertensive medications reduces the prevalence of heart attack, congestive heart failure, and stroke.

Some argue that pharmaceuticals can provide a relatively low-cost alternative to other available medical treatments. In 1989, PhRMA, then called the Pharmaceutical Manufacturers Association (PMA), estimated that between 1976 and 1985 a new drug therapy for ulcers reduced the cost of treating ulcers by $5.8 billion.[66] More often, though, pharmaceuticals complement rather than replace other forms of health care. Many surgical procedures are accompanied by pharmaceutical use both during and after surgery, and pharmaceuticals are often used to diagnose diseases that are then treated with surgery and/or medicine. In general, therefore, pharmaceuticals are not a very close substitute for most forms of medical treatments.

Overall, the extent of substitutability is fairly low. Few pharmaceuticals can be replaced by nonpharmaceutical products and services, although more than one pharmaceutical product is often available to treat a given ailment. The degree of substitution in the prescription drug market increases over time as patents expire and generic equivalents enter the market. Substitution is highest in the OTC market where market entry is relatively easy.

3.3.2.5 Price Elasticity of Demand

Few econometric studies have attempted to measure empirically the effect of price on the demand for pharmaceuticals (i.e., the price elasticity of demand). Four such studies have been published,[67] although only one was conducted in the United States. Their elasticity estimates are presented in Table 3-17, and the results are discussed below.

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[66] Pharmaceutical Manufacturers Association (PMA), 1989. *Pharmaceutical Manufacturers Association Annual Report.*

[67] Reekie, Duncan W., 1978. Price and Quality Competition in the United States Drug Industry. *The Journal of Industrial Economics* 26(3):223-237; Lavers, R.J., 1989. Prescription Charges, the Demand for Prescriptions and Morbidity. *Applied Economics* 21:1043-1052; O'Brien, Bernie, 1989. The Effect of Patient Charges on the Utilization of Prescription Medicines. *Journal of Health Economics* 8:109-132; Johnston, 1991. As cited in RTI, 1993. *Op cit.*

Table 3-17

Estimates of the Price Elasticity of Demand for Prescription Drugs

Study Author	Elasticity Estimates	Study Time Frame	Comments
Reekie, 1978. *Op. cit.*	-1.03 to -2.83	1958-1975	Study of individual pharmaceutical products within 25 therapeutically competitive markets. Price of close substitutes included in regression estimate. Calculated separate estimates for therapeutically significant and insignificant drugs.
Lavers, 1989. *Op. cit.*	-0.15 to -0.20	1971-1982	Study of increases in prescription charges for a wide range of pharmaceuticals in the U.K.
O'Brien, 1989. *Op. cit.*	-0.23 -0.64	1969-1977 1978-1986	Study of increases in prescription charges for a wide of range of pharmaceuticals in the U.K.
Johnston, 1991. *Op. cit.*	-0.5	NA	Study of increases in prescription charges for a wide range of pharmaceuticals in Australia.

NA = Not Available.

In separate studies, O'Brien and Lavers estimated the effect on demand for a wide range of prescription drugs given an increase in the copayment demanded by Great Britain's National Health Service (NHS).[68] Between 1969 and 1986 the charge for prescription drugs increased substantially in Great Britain from 0.125£ per prescription in 1969 to 2.20£ in 1986 (£1986), an increase in real terms by a factor of 17.6. The ratio of patient charges to actual drug cost also more than doubled over that same time period from 0.21 in 1969 to 0.43 in 1986. The patient charge was a fixed rate and did not vary by prescription type. Men over the age of 65, women over the age of 60, children under 16, and low income groups were exempt from the prescription charges. Approximately 24 percent of the 323 million prescription items dispensed in 1986 included an associated charge.

Both O'Brien and Lavers found a negative relationship between prescription charges and the volume of nonexempt prescription items dispensed. O'Brien's study estimated a price elasticity of demand over the entire period of -0.33, indicating that a 1 percent increase in patient charges leads to a 0.33 percent decrease in prescription drug use. O'Brien also discovered that there has been a gradual change over time in the elasticity. For the period 1969 to 1977, O'Brien calculated a price elasticity of -0.23. Elasticity increased in his study, however, to -0.64 between 1978 and 1986. This finding suggests that prescription drug use became more responsive to price between the study periods. Using similar data, Lavers found an elasticity of demand between -0.15 and -0.20 for the period 1971 to 1982, remarkably close to O'Brien's 1969-1978 estimate.

Johnston studied a similar situation in Australia where federal policies led to a doubling of prescription charges for a large group of pharmaceuticals in the 1970s.[69] Johnston's estimate of -0.5 indicates slightly more elastic demand than indicated by studies by O'Brien and Lavers.

The studies conducted by O'Brien, Lavers, and Johnston do not consider the possibility of substitution among drug products within specific therapeutic markets, and thus do not provide a complete measure of demand elasticity for individual drug products. Reekie accounts for product substitution by including the price of therapeutically competing drugs in the estimating equations for individual prescription

[68] O'Brien, 1989. *Op. cit*.; Lavers, 1989, *Op. cit.*

[69] Johnston, 1991. *Op. cit*.

drugs within therapeutic categories.[70] Using this method, Reekie found more elastic demand than either O'Brien, Lavers, or Johnston. Reekie's estimates ranged from -1.03 to -2.83, depending on the therapeutic significance of the drug and how many years the drug had been on the market. Predictably, Reekie's estimates were most elastic for drugs that had been on the market for a number of years and offered only modest therapeutic gains, and most inelastic for recently introduced drugs that provided important therapeutic gains.

Although these empirical studies are hardly conclusive regarding price elasticity, they do indicate that the demand for pharmaceuticals as a group may be quite inelastic (i.e., between 0 and -1.0), whereas the demand for a specific drug product may be relatively elastic (i.e., less than -1.0). The absence of close substitutes for drug therapies in general and the presence of health insurance leads one to expect that the overall demand for pharmaceuticals would be inelastic. Conversely, given the existence of close substitutes for individual drugs (e.g., generics and other therapeutically similar drugs) and the pressure to control health care costs, the demand for specific drugs may be relatively price elastic.

3.3.3 Market Conduct and Performance

To predict regulatory impacts, it is necessary to examine not only how the pharmaceutical industry is structured, but how it behaves. The pharmaceutical industry has been under attack for its seemingly uncompetitive pricing tactics, for having excessive market power related to patent protection advantages, and for other potential barriers to entry discussed above. This section explores the numerous factors pharmaceutical manufacturers consider when setting drug prices, examines the evidence on drug price inflation, and discusses some of the recent actions taken by both industry and government to control drug prices.

A basic element of market performance is the rate of price inflation. The price of drugs has outpaced the rate of general inflation over the last several decades. Table 3-18 presents producer price indices (PPI) for selected drug categories including all drugs, single-source drugs, and multiple-source drugs for selected years between 1981 and 1988. As can be seen in the table, the rate of increase in the PPI for almost all drug types outpaced inflation (i.e., the change in PPI for all commodities) in the 7 years studied.

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[70] Reekie, 1978. *Op. cit*.

Table 3-18

Change in Producer Price Index for Pharmaceuticals: 1981-1988

Commodity	Percent Change in PPI 1981-1988	Average Annual Percent Change in PPI	Annual Percent Change in PPI						
			1982	1983	1984	1985	1986	1987	1988
All commodities	9.1	1.3	2.0	1.3	2.4	-0.5	-2.9	2.6	4.0
All drugs	83.5	9.1	7.3	9.5	9.6	9.6	8.7	8.7	10.1
Single-source drugs	78.1	8.6	7.6	7.3	9.8	10.2	8.1	7.3	9.9
Multiple-source drugs	85.8	9.3	7.2	10.4	9.5	9.3	9	9.4	10.1
Originator	105	10.8	8.9	12.9	11.5	10.5	10.4	10	10.9
Non-originator	20	2.7	2.1	0.7	-0.5	3.3	2.1	4.7	6.3

Source: HCFA, 1992. Health Care Financing Administration. Pharmaceutical Price Changes: 1981-1988. *Health Care Financing Review* 14(1): 90-105. Fall 1992.

A General Accounting Office report, however, indicates that the government's index overstated drug inflation between 1984 and 1991 by 23 to 36 percent due to a failure to take into account the impact of new, recently introduced medicines.[71] Recent PPI data from the Bureau of Labor Statistics seems to support this idea. According to the Bureau of Labor Statistics, the PPI for pharmaceuticals has been under 10 percent since 1989 and has steadily declined–so much so that the PPI for pharmaceuticals approached the general rate of inflation in 1994 (see Table 3-19). Some have viewed these statistics as indicating that market pressures are working to moderate drug prices. Indeed, the U.S. Department of Commerce has noted that market pressures have led 10 of the leading pharmaceutical firms to promise to increase their average prices at a rate no greater than the general inflation rate.[72]

Even the higher levels of drug price inflation in previous decades have not matched the inflation rate for medical care generally. Table 3-20 lists consumer price indices (CPI) for medical care generally, prescription drugs, hospital rooms, and physician services between 1950 and 1985. According to these data, the CPI for drugs rose 187 percent between 1950 and 1985, in contrast to the much larger CPI increases in medical care (651 percent between 1950 and 1985) and hospital rooms (2,245 percent between 1950 and 1985) over the same time period. Interestingly, between 1950 and 1985, the CPI for drugs rose less than the rate of inflation (i.e., the change in CPI for all goods and services). In 1986 through 1992, however, the CPI for drugs increased approximately twice as much as the general rate of inflation in most years (see Table 3-21). More recently, the CPI for prescription drugs has increased more closely to the rate of inflation. Over the years 1986 through 1997, CPI for drugs increased by 91 percent compared to 46 percent associated with CPI for all items, or roughly double the rate of inflation..

3.3.3.1 Patterns of Price Competition

Manufacturers have considerable latitude to set prices according to factors other than marginal cost, such as reputation, demand conditions in different markets (e.g., hospital v. retail), and the company's long-

[71] U.S. General Accounting Office (GAO), 1995. *Prescription Drug Prices*: *Official Index Overstates Producer Price Inflation*. Washington, DC: U.S. GAO.

[72] U.S. Department of Commerce, 1994. *Op. cit.*

Table 3-19

Change in Producer Price Index for Pharmaceuticals: 1988-1997

Commodity	Percent Change in PPI 1988-1997	Average Annual Percent Change in PPI	Annual Percent Change in PPI								
			1989	1990	1991	1992	1993	1994	1995	1996	1997
All commodities	19.4	2.0	5.0	3.7	0.2	0.6	1.5	1.3	3.5	2.4	-0.1
All drugs (SIC 283)	47.6	4.3	7.7	6.4	6.5	6.1	4.0	1.4	2.4	1.8	2.0

Source: http://146.142.4.24/cgi-bin/surveymost

Table 3-20

Change in Consumer Price Index for Pharmaceuticals and Selected Health Care Services: 1950-1985

Year	Percent Change from Previous Year				
	All Goods and Services (%)	**Prescription Drugs (%)**	**Medical Care (%)**	**Hospital (Semiprivate Room) (%)**	**Physician Services (%)**
1950	NA	NA	NA	NA	NA
1955	9.4	9.7	20.7	39.6	18.5
1960	10.4	13.5	22.1	35.5	17.7
1965	6.4	-11.5	13.1	32.5	14.7
1970	23.2	-0.8	34.7	91.6	37.5
1975	38.7	8.0	39.8	62.4	39.5
1980	53.2	41.6	57.7	77.4	59.0
1985	30.6	71.5	51.6	69.6	48.1
1950-1985	**339.2**	**186.7**	**650.7**	**2,244.9**	**622.5**

NA = Not Available

Source: Feldstein, Paul J., 1988. *Health Care Economics*. 3rd Edition. New York, NY: John Wiley & Sons.

Table 3-21

Pharmaceutical and General Inflation Indicators: 1986-1997

Year	CPI for All Items (%)	CPI for Prescription Drugs (%)	CPI for Medical Care (%)
1986	1.1	9.0	7.7
1987	4.4	8.0	5.8
1988	4.4	7.8	6.9
1989	4.6	9.5	8.5
1990	6.1	9.9	9.6
1991	3.1	9.4	7.9
1992	2.9	5.7	6.6
1993	2.7	3.3	5.4
1994	2.7	3.3	4.9
1995	2.5	2.0	3.9
1996	3.3	3.4	3.0
1997	1.7	2.6	2.8
% change from 1986 to 1997	**46%**	**91%**	**92%**

Source: Council of Economic Advisors, 1998. *Economic Report of the President: 1998.* Washington, DC: U.S. Government Printing Office; U.S. Bureau of the Census, 1997. *Statistical Abstract of the United States, 1997.* Washington, DC; U.S. Government Printing Office.

run financial goals.[73] Ultimately, the prescription drug manufacturer must establish a price that can recover the long-run costs associated with pharmaceutical R&D. Typically, manufacturers of patented drugs will set initial price well above marginal cost with the understanding that demand for the product will most likely be fairly inelastic at least until the patent expires and close substitutes become available. The manufacturer uses the time between market launch and patent expiration to recoup R&D costs and generate sufficient profits to finance new product development. The prescription drug manufacturer will devote considerable resources to promoting its product during this period, convincing physicians and patients of the drug's therapeutic benefits and establishing itself as the supplier of the drug in anticipation of generic competition.

Once the patent expires for a given prescription drug, price competition becomes a greater consideration. Because patented drugs will have garnered a certain level of brand loyalty from physicians, generic drug manufacturers must enter the market with a relatively low price to establish market share. According to NatWest Investment Banking Group, which monitors the generic industry, the first generic manufacturer to enter a given market generally prices its drug around 30 percent below the brand-name drug and realizes a gross margin of about 55 percent. The second generic manufacturer to enter a market usually prices its product at about a 40 percent discount, and the third entrant at about a 50 percent discount. NatWest estimates that by the time the fourth generic manufacturer enters a market, generics prices are half of brand-name prices and gross margins will have fallen to 30 percent or less.[74] The advantage of being the first generic entrant in a given market is clear.

Contrary to expectations, manufacturers of branded drugs do not attempt to deter entry into their markets by competing with generics on the basis of price. Rather, studies show that in most cases pioneer firms continue to increase prices following entry at the same rates as before patent expiration. Some industry experts believe that brand-name drug manufacturers do not have the same force or breadth of product line to compete with the major generic manufacturers on the basis of price.[75] Branded manufacturers trust that despite the relatively high price of their drug, physicians will continue to prescribe their drug over generic

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[73] Evidence suggests that because of the wide availability of close substitutes in the OTC drug market, OTC drug manufacturers generally act as price takers. It is assumed, therefore, that OTC prices approximate marginal cost.

[74] NatWest, 1992. *Op. cit.*

[75] *Ibid.*

drugs because they are familiar with it and because many question the quality of generic drugs even though they have been deemed bioequivalent by FDA. Nonetheless, studies show that branded drugs lose market share rapidly following patent expiration. According to one study, brand-name drug market shares decline to only 40 percent within 5 years following patent expiration.[76] Within 6 years, brand-name drugs command only 20 percent of the market. In its study of the industry, OTA made various market analyses using an assumption that within 10 years brand-name drugs will have left the market altogether.[77]

Because branded drugs lose market share so rapidly after patent expiration, and because cost pressures are encouraging even heavier reliance on generics once they become available, many major pharmaceutical firms that previously specialized in new drug development and marketing are now establishing divisions or subsidiaries that manufacture and market generic versions of their own branded products—or they are purchasing or affiliating with previously independent generics firms.[78] In this way, these companies are keeping in house product sales (albeit at a lower margin than branded product sales) that otherwise would go to outside generics manufacturers. Moreover, major innovative firms selling generic versions of their own branded products may have a competitive advantage over small independent generics firms because:

- Pharmacists may be more likely to buy generic formulations from brand-name manufacturers because they know the generics will be exactly the same as the brand-name products (rather than equivalents that other firms have developed).

- Innovative firms already have study data, bulk chemical sources, and manufacturing processes in place, so they may be able to submit ANDAs and bring generics to market more quickly and less expensively than can small independent firms.

- Innovative firms have more money than small independent firms to spend on developing and producing generics.[79]

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[76] Grabowski, 1992. *Op. cit.*

[77] OTA, 1993. *Op. cit.*

[78] Ukens, 1994. *Op. cit.;* Giltenan, 1994. *Op. cit.*

[79] Ukens, 1994. *Op. cit.*

For these reasons, the trend toward generics manufacturing by major pharmaceutical firms may threaten the survival of some generics firms, especially the smaller ones. In addition, increasing domination by major pharmaceutical manufacturers could increase their market power, permitting them to set higher prices for their generics—at 20 percent below the price of the branded product, for example, rather than the more usual 30 percent discount for a first generic entrant. Given the pressure to keep prices down, however, major pharmaceutical firms are not expected to increase the price of generics very substantially.[80] A more recent report in the Wall Street Journal seems to substantiate this prediction, noting that intense competition among generics firms (as well as between generics firms and large pharmaceutical firms) appears to be keeping drug prices in check, in one case driving down a product price by 90 percent.[81] This report noted that this level of competition is hurting some generics firms, although those in niche markets or with other products having little competition are faring quite well.

3.3.3.2 Government Actions to Limit Pharmaceutical Price Increases

In the last several years, industry as well as state and federal governments have taken measures to control drug price inflation. As noted above, for example, 10 companies with over 40 percent of the U.S. pharmaceutical market share agreed in 1990 to keep drug prices in line with inflation.[82] PhRMA, which has spearheaded the effort, continues to enlist new companies in the price control program. Today, 16 pharmaceutical companies in all have agreed to keep increases in the price of their products at or below the rate of inflation.

Federal and state governments have recently taken steps to control drug prices through the Medicaid system. Medicaid provides health insurance for U.S. citizens of limited financial means and is funded jointly by states and the federal government. Medicaid currently covers outpatient prescriptions in 49 states and the District of Columbia, and accounts for nearly 15 percent of all outpatient prescription drug expenditures in

[80] Ukens, 1994. *Op. cit.*

[81] Eisinger, 1996. *Op. cit.*

[82] Solomon, Jolie, 1993. Drugs: Is the Price Right? *Newsweek*. March 8, 1993. pp. 38

the U.S. today.[83] Retail pharmacies dispense prescriptions at little or no cost to Medicaid recipients. State Medicaid agencies then reimburse pharmacies according to specified price tables. Some 22 states require copayments ranging between $0.50 and $3.00 per prescription.[84] States must cover all drugs approved by the FDA.

The 1990 Omnibus Budget Reconciliation Act (PL 10 1-508) altered state Medicaid reimbursement policies. Prior to 1990, state Medicaid agencies reimbursed pharmacies according to the pharmacy's acquisition cost plus a reasonable markup for single-source drugs, at no more than 150 percent of the lowest published price for multiple-source drugs.[85] In 1990, however, Medicaid instituted a new reimbursement scheme whereby pharmaceutical manufacturers must give state Medicaid agencies a rebate on their drug purchases. The rebate is designed to keep the cost of Medicaid drugs at or below the rate of inflation. Beginning in 1994, Medicaid instituted more stringent reimbursement policies that created strong disincentives for manufacturers to introduce drugs at above-average prices. The law can reduce revenues for manufacturers in the Medicaid segment of the pharmaceutical market. Any health care reform or changes made as part of federal budget debates could significantly alter federal or state administration of Medicaid and might include new incentives for controlling health care costs generally and drug costs in particular.

The general trend toward cost-containment in the health care field appears to have increased—and is likely to continue to increase the level of price competition in the prescription drug market. Thus, administrative actions as well as consumer and market behavior combine to determine pricing patterns in the industry.

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[83] OTA, 1993. *Op. cit.*

[84] *Ibid.*

[85] Single-source drugs are those available from only one manufacturer (i.e., a patented name-brand drug). Multiple-source drugs are available from several manufacturers (i.e., generics).

3.3.4 Conclusions About EA Assumptions on Cost Passthrough Potential

Because regulatory costs associated with the Final Pharmaceutical Industry Effluent Guidelines can affect a large portion of the industry, the industry as a whole might be able to pass through regulatory costs to the consumer in the form of higher drug prices. Individual companies (especially those marketing generic and OTC drugs), however, will have less latitude to raise prices to the extent that their competitors do not face the same regulatory costs. Nevertheless, many companies appear to have sufficient market power to pass through regulatory costs.

The price elasticity data also suggests that at least some of the regulatory costs can be passed on to consumers. The price elasticity studies indicate that demand is highly inelastic in the case of patented drugs with no substitutes (in the range of -0.2 to -0.4), mildly inelastic for generic drugs (-0.6 to -0.8), and elastic for OTC drugs (less than -1.0). Thus, if the EA distinguished among these three market segments, regulation-induced price increases in each component of the industry could be examined. Product-specific cost and price data were, however, not available from the Section 308 Pharmaceutical Survey, thus the EA can examine impacts only on the drug market as a whole.

Despite the evidence relating to market power and price elasticities, the EA primarily will use the conservative assumption that manufacturers cannot pass through compliance costs except when impacts on consumers are investigated. In this latter case a 100 percent cost passthrough assumption is used. The assumption of no cost passthrough maximizes the estimated regulatory impacts on manufacturers, whereas an assumption of 100 percent cost passthrough maximizes the estimated regulatory impacts on consumers.